Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Review of national rare disease strategies in selected countries – Appendix B

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Appendix B. Extracted data.

Table B1. Data extracted for Australia (National Strategic Action Plan for Rare Diseases).

Australia	Strategy information
Author(s) **Title**	Australian Government Department of Health National Strategic Action Plan for Rare Diseases[22]
Timeline	Published February 2020
Overall aim(s)	**Vision** The best possible health and wellbeing outcomes for Australians living with a rare disease. **Critical Enablers** (of effective rare diseases policy) ▪ Multi-stakeholder involvement and engagement ▪ Collaborative governance and leadership ▪ State, national and international partnerships ▪ High quality, comprehensive collection, and effective use, of rare disease data. **Pillars:** 1. Awareness and Education 2. Care and Support 3. Research and Data. These **Principles** are the foundation for this Action Plan: ▪ Person-centred ▪ Equity of access ▪ Sustainable systems and workforce.
Themes and or priorities	**Pillar 1: Awareness and Education** Priority 1.1: Increase every Australian's awareness of rare diseases including, where applicable, relevant prevention measures. Priority 1.2: Ensure Australians living with a rare disease have access to information and education that enables them to be active participants in their rare disease journey. Priority 1.3: Develop a national rare disease workforce strategy that responds to current and future demands, including the impact of genomics. **Pillar 2: Care and Support** Priority 2.1: Provide rare disease care and support that is integrated and appropriate for all Australians living with a rare disease, while being both person and family-centred. Priority 2.2: Ensure diagnosis of a rare disease is timely and accurate. Priority 2.3: Facilitate increased reproductive confidence. Priority 2.4: Enable all Australians to have equitable access to the best available health technology. Priority 2.5: Integrate mental health, and social and emotional wellbeing, into rare disease care and support.

	Pillar 3: Research and Data Priority 3.1: Enable coordinated and collaborative data collection to facilitate the monitoring and cumulative knowledge of rare diseases, informing care management, research and health system planning. Priority 3.2: Develop a national research strategy for rare diseases to foster, support and drive all types of research for rare diseases, contributing to agreed priorities and systematically addressing gaps. Priority 3.4: Translate research and innovation into clinical care; clinical care informs research and innovation. **Priority Populations** ▪ Australians living with a rare disease ▪ Australians living with an undiagnosed rare disease ▪ Australians with an increased chance of developing a rare disease or of having a child with a rare disease ○ hereditary (genetic) ○ non-hereditary, related to pregnancy ○ non-hereditary, unrelated to pregnancy. ▪ Aboriginal and Torres Strait Islander people ▪ People living in regional, rural and remote areas ▪ People from culturally and linguistically diverse (CALD) backgrounds ▪ People experiencing socio-economic disadvantage ▪ Partnerships, including: ○ individuals, carers and families ○ communities ○ all levels of government ○ non-government organisations ○ the public and private health sectors, including all healthcare providers and private health insurers ○ industry ○ researchers and academics.
Targets (if specified) and measurement method(s) (where available)	*Not mentioned. See section on 'Achieving Progress' under 'Implementation' for measures of progress.*
Implementation action(s), lead(s) and key performance indicator(s)	**Action 1.1.1 Develop and conduct national awareness and education activities for rare diseases** ▪ **1.1.1.1.** Analyse existing resources and distribution and build on these to continue media and communications and material that promotes and distributed the latest information relating to rare disease. Responsibility for deliverables will be identified as art of this process. ▪ **1.1.1.2**. Ensure national media and communications material highlights challenges common across rare diseases. Market research will determine key messaging and how material is delivered. For example, it may be grouped for all rare diseases or tailored for individual rare diseases. ▪ **1.1.1.3.** Address urgent funding gaps for rare disease organisations to enable them to sustain and expand upon current awareness and education activities. These may include hosting information sessions, workshops, conferences or sending e-newsletters.

	▪ **1.1.1.4.** Collaborate with targeted stakeholder to maximise the reach and appropriateness of materials to Aboriginal and Torres Strait Islander people, those with CALD backgrounds, and other priority populations. **Action 1.1.2 Raise awareness of, and deliver, relevant prevention measures for non-hereditary rare diseases, such as cancers, infections and autoimmune disorders.** ▪ **1.1.2.1.** Governments, healthcare services and stakeholder organisations raise awareness of, and educate about, relevant prevention measures for non-hereditary rare diseases, including through national and localised media and communications material. ▪ **1.1.2.2.** Governments and healthcare services deliver relevant prevention measures to reduce the incidence of non-hereditary rare diseases. An example is activity targeted at geographic locations with low whopping cough vaccination rates. **Action 1.1.3 Develop, deliver and promote targeted awareness and education activity to support people in their preparation for conception and pregnancy.** ▪ **1.1.3.1.** Governments and healthcare services raise awareness of rare diseases and educate people preparing for conception and pregnancy. This is incorporated into existing preconception and perinatal care. This could include education and awareness pertaining to both preventative measures and rare diseases testing and screening opportunities such as: ○ preconception (carrier) testing and screening ○ preimplantation genetic diagnosis (testing) and screening ○ antenatal testing and screening ○ newborn testing and screening. ▪ **1.1.3.2.** Governments and healthcare services support people in their preparation for conception and pregnancy through evidence based, high-quality pre-conception and antenatal care, including vaccinations. An example is educating women of child-bearing age about the benefits of vaccination against Rubella (German measles) prior to conception to prevent the development of congenital abnormalities. ▪ **1.1.3.3**. Develop and promote non-directive education materials for use by individuals and families following access to the range of genetic testing or screening opportunities for rare diseases. These materials are to be developed in partnership with healthcare professionals and the public to identify the ethical, legal, social and other issues families may wish to take into consideration. **Action 1.2.1 Raise awareness among people living with a rare disease, and their families and carers, about the care and support services available to them.** ▪ **1.2.1.1.** Develop and maintain an accessible multi-purpose digital repository to detail available care and support services and to provide general rare diseases information. The repository can be used to identify gaps and opportunities for improvement. Promote the repository to rare disease organisations, for distribution to people living with a rare disease, and their families and carers. ▪ **1.2.1.2.** Build on existing activities of rare disease organisations and raise awareness of care and support services available to people living with a rare disease, and their families and carers. Identify gaps and opportunities for improvement. **Action 1.2.2 Improve consultation and communication between policy-makers and the rare disease community.** ▪ **1.2.2.1.** Rare disease organisations strengthen their connections with policy-makers. This would build on current coordination by existing national and state-based collaborations. ▪ **1.2.2.2.** Further articulate the consumer voice through the facilitation of an advisory group to improve consultation and communication on a range of issues including disability, health, housing, education and employment.

	Action 1.3.1 Develop a national rare disease workforce strategy. ▪ **1.3.1.1.** Identify existing gaps in the workforce that support people living with a rare disease and outline a path towards a sustainable workforce, taking into account the impact of genomics. ▪ **1.3.1.2.** Ensure collaboration and consultation occurs between implementation Partners, including education providers, professional bodies, and other key stakeholders. ▪ **1.3.1.3.** Ensure the strategy includes measures to empower practitioners to provide culturally safe and appropriate care and support to Aboriginal and Torres Strait Islander people, those with CALD backgrounds, and other priority populations. **Action 1.3.2 Equip and encourage frontline health professionals to consider, investigate and refer for a potential rare disease diagnosis.** ▪ **1.3.2.1.** Develop and promote guidelines for Australia in line with the International Joint Recommendations to Address Specific Needs of Undiagnosed Rare Disease Patients. These guidelines will provide support for clinicians in identifying possible rare disease in people who present with complex symptoms. They will also articulate the key role that health professionals play in meeting the support needs of individuals and families through the diagnostic journey. ▪ **1.3.2.2.** Through relevant professional peak bodies, promote the use of the accessible multi-purpose digital repository by health professionals. This will support health professionals to consider a rare disease diagnosis when people present with complex and unexplained symptoms. ▪ **1.3.2.3.** Develop awareness and education that empowers frontline health professionals to provide culturally safe and appropriate care and support to Aboriginal and Torres Strait Islander people, those with CALD backgrounds, and other priority populations. **Action 2.1.1 Provide rare disease care and support that is integrated, incorporating clear pathways throughout health, disability and other systems.** ▪ **2.1.1.1.** Establish standards for care and support that are integrated and incorporate clear pathways throughout all systems. Ensure these are informed by clinical and consumer rare disease experts and that such consultation informs policy development. ▪ **2.1.1.2.** To reduce fragmented care, ensure policy meets people's full range of need, inducing health, disability and education. Support this work with a cross-jurisdictional, cross-sectoral working party. ▪ **2.1.1.3.** Increase the utilisation of digital health, including virtual clinics and telehealth (telemedicine) services. Leverage existing infrastructure, such as My Health Record, to support care and improve integrations. ▪ **2.1.1.3**. Increase the utilisation of digital health, including virtual clinics and telehealth (telemedicine) services. Leverage existing infrastructure, such as My Health Record, to support care and improve integration. ▪ **2.1.1.4.** Ensure care and support responsive to the specific needs of rural and remote communities and health services, Aboriginal and Torres Strait Islander people, those with CALD backgrounds, and other priority populations. **Action 2.1.2 Build a broad range of care and support services that are responsive to the changing needs of people living with a rare disease and their families.** ▪ **2.1.2.1.** Develop an accessible multi-purpose digital repository, incorporating elements targeted at the workforce that supports people living with a rare disease. With access to adequate information, healthcare and social support professionals will be equipped to support people living with a rare disease and their families to navigate health, disability and other systems.

	▪ **2.1.2.2.** Strengthen the National Disability Insurance Agency's response to the nature of disability caused by rare disease that can manifest as chronic, intermittent and often progressive. Initial implantation should prioritise: ○ fast tracking access to the NDIS ○ ensuring NDIS participants can access an appropriate range of respite to meet the needs of families. ▪ **2.1.2.3.** Through regular stakeholder consultations, determine strategies to improve access to rare disease care and support services for Aboriginal and Torres Strait Islander people, those with CALD backgrounds, those living in rural and remote areas, and other priority populations. **Action 2.1.3 Ensure services support people living with a rare disease through significant life-stage transitions.** ▪ **2.1.3.1.** Enhance existing transition services to ensure people living with a rare disease experience seamless transitions between services as they move through life stages. Common transitions include: ○ reaching the age cut-off point for paediatric services (for example, transitioning for child to adult hospitals) ○ relocating ○ when needs change significantly (such as the end-of-life). ▪ **2.1.3.2.** Increase awareness among health and other professionals, and rare diseases organisations of the multi-faceted role of palliative care, including peri-natal palliative care. Palliative care can achieve a range of objectives for people and families living with rare disease, including improving quality of life and providing end-of-life care. This will assist to improve: ○ uptake of palliative care by people living with a rare disease or by families who may benefit from peri-natal palliative care ○ timeliness of referrals by health professionals. ▪ **2.1.3.3.** Promote the specific needs of people living with life-limiting rare disease to the palliative care sector. ▪ **2.1.3.4** Ensure transition services are culturally safe and appropriate, in recognition of unique life-stage challenges faced by Aboriginal and Torres Strait Islander people. **Action 2.1.4 Develop the capacity of rare disease organisations to represent and advocate for people living with a rare disease and their families.** ▪ **2.1.4.1.** Rare disease organisations represent and advocate for people living with a rare disease and their families through a range of activities including: ○ written submissions ○ consumer hearings ○ communicating with their community ○ representing their community to stakeholders, such as government and industry ○ advocating for reimbursement of health technologies after independent health technology assessment (HTA) has demonstrated effectiveness. Further support the current activities of rare disease organisations trough additional resourcing as well as further national collaboration. ▪ **2.1.4.2.** Ensure consultation with targeted stakeholders to strengthen the capacity of rare disease organisations to appropriately represent and advocate for Aboriginal and Torres Strait Islander people living with a rare disease and their families. **Action 2.1.5 Embed the voice of people living with a rare disease and their families and carers throughout structures and systems that impact rare diseases.** ▪ **2.1.5.1.** Capture and promote the voice of people living with a rare disease and their families and carers by:

	○ involving people living with a rare disease at every level of decision-making; ○ ensuring ongoing engagement to capture broader input from people living with a rare disease through surveys, focus groups, newsletters and representation on boards; and ○ calling for key structures and systems to routinely and effectively capture broader input from consumers, as done currently in some research settings and HTA (consumer hearings). ▪ **2.1.5.2** Enhance culturally safe and appropriate approaches for Aboriginal and Torres Strait Islander people, including aligning with existing initiatives to develop and implement ways to integrate Indigenous Australian languages to equitably enhance care and support. **Action 2.2.1 Ensure all Australians have equitable access to a range of diagnostic tools and tests, providing the best chance of early and accurate diagnosis.** ▪ **2.2.1.1.** Further the development of, and investment into, the range of existing specialist diagnostic responses, such as genomics technology, including for Aboriginal and Torres Strait Islander people; interdisciplinary undiagnosed disease programs, clinical phenotype diagnostic support tools; centres of expertise; genetic counsellors and peer support groups. ▪ **2.2.1.2.** Ensure all existing screening and testing programs are sustainable and evolve in line with innovation over time. ▪ **2..2.1.3.** Enhance culturally safe and appropriate approaches for Aboriginal and Torres Strait Islander people, including aligning with existing initiatives to develop and implement way to integrate Indigenous Australian languages to equitably enhance diagnosis. **Action 2.2.2 Develop policy that supports the implementation of diagnostic tools and tests.** ▪ **2.2.2.1.** Support national leadership and coordination of a range of screening and diagnostic tools and tests jointly funded by Commonwealth and state/territory governments, to enable more consistent service and equitable access. ▪ **2.2.2.4.** Develop non-directive education materials for use by individuals and families following access to genetic testing. These materials are to be developed in partnership with healthcare professionals and the public to identify the ethical, legal, social and other issues that individuals and families may wish to take into consideration in their decision-making. ▪ **2.2.2.5** Develop comprehensive, best-practice support standards and materials that address the diverse possibilities that may arise from individuals and families undertaking genetic testing. **Action 2.2.3 People with an undiagnosed rare disease are identified and have priority access to the most appropriate specialised and expert diagnostic response.** ▪ **2.2.3.1.** Flag in health information systems when someone presents with an undiagnosed rare disease. ▪ **2.2.3.2**. Develop guidelines for Australia in line with the International Joint Recommendations to Address Specific Needs of Undiagnosed Rare Disease Patients. This will provide support for clinicians in: ○ identifying possible rare disease in people who present with complex symptoms ○ outlining best practice and timely diagnostic pathways for example, including best practice around reducing wait times for genetic counselling appointments ○ ongoing management of the person with a suspected undiagnosed rare disease, in order to aid diagnosis. ▪ **2.3.3.3.** Increase the capacity and reach of the existing state-based best-practice undiagnosed disease program models to achieve national coverage. **Action 2.2.4 Support people with a suspected but undiagnosed rare disease on their diagnostic journey.**

	▪ **2.2.4.1.** Undertake a survey on existing support for people with an undiagnosed rare disease delivered by rare disease organisations, to identify gaps and opportunities for improvement. ▪ **2.2.4.2**. Address gaps and opportunities for improvement, identified through the survey, by funding awareness raising and support activities conducted by SWAN Australia and other relevant organisations ▪ **2.2.4.3**. Rare disease organisations collaborate to develop supporting material that describes best practice approaches to delivering this support, taking into account the great diversity of rare disease journeys. ▪ **2.2.4.4**. Ensure consultation with targeted stakeholders to maximise appropriateness of this support for Aboriginal and Torres Strait Islander people, those with CALD backgrounds, and other priority populations. **Action 2.3.1 Ensure individuals and families known to have an increased chance of being carriers of genetic variants for rare diseases have equitable access to peri-conception genetic testing and counselling, which can provide them with information about becoming pregnant and pregnancy.** ▪ **2.3.1.1.** Further to the National Health Genomics Policy Framework and Pregnancy Care Guidelines, develop consistent and comprehensive clinical guidelines for all relevant health professionals to support individuals and families to access peri-conception genetic testing, counselling and peer support groups. ▪ **2.3.1.2.** Ensure equity of access for all Australians with an increased chance of being carriers of genetic variants for rare diseases to peri-conception genetic testing and counselling. Promote connection to genetic peer support groups for further support. ▪ **2.3.1.3**. Develop non-directive education materials for use by individuals and families surrounding access to peri-conception genetic testing. These materials are to be developed in partnership with healthcare professionals and the public to identify the ethical, legal, social and other issues that individuals and families may wish to take into consideration in their decision-making. ▪ **2.3.1.4.** Continue to support individuals and families through the range of possible outcomes following peri-conception genetic testing. **Action 2.3.2 Women who have, or are at risk of developing, certain chronic conditions, such as diabetes, epilepsy or thyroid disorders, have an increased chance of having babies with rare congenital anomalies. Provide these women with access to evidence-based, high-quality pre-conception and peri-natal care.** ▪ **2.3.2.1.** Governments and healthcare services provide women planning a pregnancy with increased and equitable access to a pre-conception consultation program to investigate whether they have, or are at risk of developing, certain chronic conditions, such as diabetes, epilepsy or thyroid disorders, that may affect their pregnancy. ▪ **2.3.2.2.** Governments and healthcare services support these women to access evidence-based, high-quality pre-conception or pregnancy care and support when they are planning a pregnancy or already pregnant. This includes equitable access to the range of rare diseases testing and screening opportunities such as: ○ antenatal testing and screening ○ newborn testing and screening. ▪ **2.3.2.3.** Address urgent funding gaps in the NBS National Policy Framework for effective implementation and sustained success, including: ○ equipment costs ○ ongoing secretariat support of the NBS Program Management Committee ○ funding for the national decision-making process ○ implementation of new screening tests recommended through the national decision-making process ○ funding for monitoring and evaluation of programs

	○ national communication and education resources. **Action 2.4.1 Develop policy that supports people living with a rare disease to have timely and equitable access to new and emerging health technologies.** ▪ **2.4.1.1.** Broaden the description and understanding of the principles underpinning Australian HTA processes to acknowledge the challenges associated with assessing health technologies for rare diseases. ▪ **2.4.1.2.** Align with and build on the existing National Health Genomics Policy Framework for the systematic, equitable and timely delivery of genomic services, such as genetic testing (diagnostics) and gene therapies (treatments) and genetic counselling to Australians with, suspected of having, or with an increased chance of a rare disease. ▪ **2.4.1.3.** Develop comprehensive, best-practice support standards and materials to ensure timely delivery of high-quality care by genetic services. ▪ **2.4.1.4.** Build rare disease expertise within the Office of Health Technology Assessment (OHTA) that is responsible for analysing potential rare disease impacts. ▪ **2.4.1.5.** Ongoing review of health technology policy in line with advancements in health technology. For example, mitochondrial donation involves removing the nuclear DNA from a woman's egg containing faulty mitochondria and inserting it into a healthy donor egg, which has had its nuclear DNA removed. This prevents mitochondrial DNA defects from being inherited by a genetically related offspring. Mitochondrial donation is not yet legal in Australia. **Action 2.4.2 Ensure funding and reimbursement pathways are fit-for-purpose and sustainable for current and new health technologies for rare diseases.** ▪ **2.1.2.1.** Build on the current processes within the OHTA to ensure all rare diseases submissions are flagged as complex and may require additional scoping and engagement to address potential challenges and uncertainties. ▪ **2.4.2.2.** Raise awareness among industry and rare disease organisations as to the availability of the HTA Access Point. ▪ **2.4.2.3.** Ensure rare disease expertise exists, or can be accessed, on all reimbursement pathways and HTA advisory bodies. **Action 2.4.3 Ensure people living with a rare disease have equitable access to medicines with demonstrated clinical benefit for a rare disease, including those that are already funded for another condition.** ▪ **2.4.3.1.** Ensure the HTA Consumer Evidence and Engagement Unit provides education and support to people living with a rare disease and their families and carers, and/or rare disease organisations to support them to take a more active role in HTA processes. ▪ **2.4.3.2.** Rare disease organisations work with the HTA Consumer Evidence and Engagement Unit to submit an application for public reimbursement of a technology eligible for assessment by the OHTA. ▪ **2.4.3.3.** The TGA and OHTA continue to work together to develop clear processes and pathways for sponsors considering submitting applications for the repurposing of medicines already approved for use in treatment of other conditions. **Action 2.5.1 Ensure people living with a rare disease, including their families and carers, receive the community, clinical and digital mental health supports and services they need.** ▪ **2.5.1.1.** Enable people living with a rare disease, including their families and carers (with appropriate consent) to access information and resources (including digital) customised for rare diseases as part of Chronic Disease Management Plans and Mental Health Care Plans.

	▪ **2.5.1.2**. Ensure Aboriginal and Torres Strait Islander people living with a rare disease have access to customised resources (including digital), in recognition of the greater challenges to achieving the best possible social and emotional wellbeing support outcomes for Aboriginal and Torres Strait Islander people. **Action 2.5.2 Implement care and support systems to address the mental health and wellbeing of Australians impacted by a rare disease.** ▪ **2.5.2.1.** Empower rare disease care and support providers to deliver the best possible mental health and social and emotional wellbeing support outcomes through a range of initiatives, including: ○ access to evidence that aids providers in their understanding of and ability to respond to mental health and social and emotional wellbeing support needs, such as a rare disease mental health checklist ○ awareness around the existing range of free or low cost digital mental health services that provide support, such as Head to Health ○ education about how to access and utilise these services ○ cultural competency education that empowers providers to effectively support Aboriginal and Torres Strait Islander people. ▪ **2.5.2.2.** Provide mental healthcare that recognises the unique challenges associated with rare diseases via existing systems, such as Chronic Disease Management Plans and Mental Health Care Plans. **Action 2.5.3 Develop the capacity of rare disease organisations to provide wellbeing and mental health support.** ▪ **2.5.3.1.** Better resource existing social and emotional wellbeing support provided by rare disease organisations including: ○ peer support ○ family days ○ community engagement ○ information sessions and workshops. ▪ **2.5.3.2.** Provide education and training to rare disease organisations to increase their awareness of mental health issues and guide people to seek further support. ▪ **2.5.3.3**. Undertake targeted stakeholder consultations to ensure appropriate social and emotional wellbeing support, including appropriate referral to GPs, for Aboriginal and Torres Strait Islander people, those with CALD backgrounds, those living in rural and remote areas, and other priority populations. **Action 3.1.1 Health information systems identify and measure rare diseases and undiagnosed rare diseases.** ▪ **3.1.1.1.** The Australian Institute of Health and Welfare (AIHW) re-establishes the Australian National Congenital Anomalies Register (NCAR), including rare disease coding (ORPHAcodes). This will accelerate, extend and nationalise rare disease coding already underway in the Western Australian Register of Developmental Anomalies (WARDA), and contribute to International Classification of Diseases 11th Revision (ICD-11) preparedness. ▪ **3.1.1.2.** Develop a nationally-recognised definition of undiagnosed rare diseases in consultation with relevant experts. Using this definition, provide for an undiagnosed rare disease code in an individual's health record that is compatible with ORPHAcodes, ICD-11 and other relevant classifications. This code could: ○ raise a flag or alert to health professionals when they access the individual's health record (similar to drug allergy alerts), thus prioritising a diagnostic response ○ support data collection for undiagnosed rare diseases, and hence strategic decision-making, such as service planning.

	▪ **3.1.1.3.** Provide for rare disease codes in patient records that are compatible with ORPHAcodes, ICD-11 and other relevant classifications. This code could: ○ raise a flag or alert to health professionals when they access the individual's health records, thus leading to appropriate care that takes into account the rare disease diagnosis ○ support data collection for rare diseases, and hence strategic decision-making. ▪ **3.1.1.4.** Ensure rare disease and undiagnosed rare disease codes link with a person's Aboriginal and Torres Strait Islander status to allow for culturally appropriate care, and to build evidence of rare disease epidemiology among Aboriginal and Torres Strait Islander people. **Action 3.1.2 Undertake broad epidemiological surveillance of rare diseases to support decision-makers to access the information they need to improve the health and wellbeing of Australians living with a rare disease.** ▪ **3.1.2.1.** Building on existing newborn screening and congenital anomalies data collections, further develop Australia's monitoring of rare diseases and undiagnosed rare diseases. Examples may include and extend beyond: ○ newborn and paediatric age ranges ○ the rare diseases currently captured in newborn screening and congenital anomalies data collections. ▪ **3.1.2.2.** Establish a dedicated Rare Disease Office within the AIHW that publishes periodic national reports on the epidemiology of rare diseases and undiagnosed rare diseases in Australia, including among Aboriginal and Torres Strait Islander people. **Action 3.1.3 Improve rare disease data collection and use, including best-practice safe storage, data sharing, custodianship, analysis, reporting and privacy requirements.** ▪ **3.1.3.1.** Establish a dedicated Rare Disease Office within the AIHW. Included in its remit will be systematic improvements in rare disease data integration and interoperability. ▪ **3.1.3.2.** Publish appropriate data collected through post-market surveillance mechanisms, including under the LSDP to enable better data use and the accumulation of rare diseases knowledge. **Action 3.1.4 Develop a national approach to person-centred rare disease registries to support national standards, best practice and minimum data sets.** ▪ **3.1.4.1.** Develop a summary report of all existing Australian and relevant international rare disease registries, collecting information on: ○ governance standards ○ management practices ○ data sets, including patient numbers, estimated incidence, prevalence and coverage ○ classification systems used (for interoperability with other registries and health information systems). This information will support national coordination of rare disease registries and the establishment of minimum data sets, provide a better understanding of who is currently being counted and aid identification of best practice. ▪ **3.1.4.2.** Further develop and resource the existing RVA-led National Alliance of Rare Disease Registries to encourage collaboration, shared knowledge, standardisation, alignment with research initiatives and best practice. **Action 3.2.1 Develop a national research strategy for rare diseases, to keep pace with genomic advancements, precision medicine and innovation.**

	▪ **3.2.1.1.** Undertake a national stakeholder consultation process to set agreed priorities for a national research strategy for rare diseases, including: o surveys o public forums o targeted themed roundtables o opportunities for public submissions. ▪ **3.2.1.2**. Develop a national research strategy for rare diseases, building in regular reviews. **Action 3.2.2 Proactively address evidence gaps in areas that are important to people living with a rare disease.** ▪ **3.2.2.1.** Ensure lived experience drives research by encouraging collaboration between researchers and people living with a rare disease through workshops, conferences and consumer reference groups. ▪ **3.2.2.2.** Research funding bodies identify and report on research related to rare diseases. ▪ **3.2.2.3.** In response to limited evidence and in line with open publishing (also known as open access initiatives), share outputs from research, including publications and data. ▪ **3.2.2.4.** Prioritise and encourage fundamental discovery research for rare diseases through research funding. This is in recognition of its central importance to the development and testing of much-needed innovation in health technology for rare diseases. **Action 3.2.3 Support collaborative research into rare diseases in Australia and internationally.** ▪ **3.2.3.1.** Encourage and facilitate greater research collaboration nationally, internationally and with industry. Examples of how this may be achieved include: o financial incentives for research teams that can demonstrate collaboration with national, international and industry partners o the development of customised research grants for rare diseases that require a degree of collaboration with national, international and industry partners. **Action 3.2.4 Building on existing initiatives, continue to foster an environment conducive to clinical trials for rare diseases taking place in Australia.** ▪ **3.2.4.1.** Develop recommendations to encourage and enable more clinical trials for rare diseases to take place in Australia. ▪ **3.2.4.2.** Increase the economies of scale of research into rare diseases by, for example, operating multi-trial sites that share common resources. ▪ **3.2.4.3.** Encourage the adoption of unique and appropriate trial designs that overcome rare disease research challenges. **Action 3.2.5 Investigate and promote options that enable Australians living with a rare disease to participate in clinical trials and other research activity, both in Australia and internationally (without needing to leave Australia).** ▪ **3.2.5.1.** Identifying and maximising utilisation of available resources and assets to the extent possible, link people living with a rare disease to research activity, such as data collection, registries, natural history studies, qualitative research and clinical trials based in Australia and internationally. ▪ **3.2.5.2**. Investigate and promote options for a Trials Enabling Program for trials for rare diseases in Australia, leveraging a partnership approach that involves philanthropy and industry in the absence of relevant clinical trials in Australia.

	Action 3.3.1 Provide people living with a rare disease or an undiagnosed rare disease with the opportunity and support to participate in research. ▪ **3.3.1.1.** Health professionals inform and connect people living with a rare disease to research as part of their ongoing care. ▪ **3.3.1.2.** Develop opportunities for individuals to share their lived experience to contribute to research. Rare disease organisations can promote this by increasing their liaison with researchers and clinicians, and by disseminating information. ▪ **3.3.1.3.** Promote culturally safe and appropriate approaches for Aboriginal and Torres Strait Islander people. **Action 3.3.2 Enable researchers, funders and policy-makers to access the voice of people living with a rare disease in driving and delivering research into rare diseases.** ▪ **3.3.2.1.** Develop and support consumer reference groups to promote additional pathways for researchers, research funders, policy-makers and other decision-makers to be informed about the rare disease community's needs and priorities. Wherever possible, leverage and build on the expertise and resources of existing groups and mechanisms. ▪ **3.3.2.2.** The rare disease sector promotes the importance of a person-centred approach to research, and the mechanisms to achieve this, including co-design. **Action 3.4.1 Support partnerships between researchers and clinicians in research into rare diseases.** ▪ **3.4.1.1.** Research funding bodies prioritise research proposals and applications for rare diseases that can demonstrate support from, and close working relationships with, clinicians. ▪ **3.4.1.2.** Support and foster interdisciplinary research teams to encourage more person-centred research, and a dual focus on research and clinical care where appropriate. **Action 3.4.2 Identify, leverage and enhance existing capability and infrastructure to ensure appropriate and experienced resourcing is available within clinical teams that deliver rare disease care.** ▪ **3.4.2.1.** In partnership with industry, philanthropy and trial sites, identify and enhance existing capability and infrastructure within clinical centres to ensure appropriate capability is available to support the operation of clinical trials for rare diseases. ▪ **3.4.2.2.** Support clinical teams to collect and input data, contributing to research and evidence-building. **Achieving Progress** This Action Plan and its Priorities, Actions and Implementation activity has been informed by stakeholder consultation with the rare disease sector, from which a number of key themes emerged. The Action Plan has been developed 'by the rare disease sector, for the rare disease sector'. The themes detailed below will become its measures of progress over time. **Theme #1: The need for national leadership, coordination and consistency.** This theme emerged most frequently from the consultation process, with participants calling for: ▪ **A national plan for Australia that is in line with global standards:** Australia remains in danger of falling further behind many countries already tackling rare diseases through policy and legislation. This Action Plan is an opportunity for Australia to adopt a national plan for rare diseases that aligns with global standards. The value of a nationally coordinated plan cannot be underestimated. ▪ **Annual implementation plan:** Existing plans for rare diseases, including those in Europe and the UK, are accompanied by an implementation plan. In Australia, this plan should be developed collaboratively by the sector and could be led by the existing national peak body for rare diseases. Progress in implementation should be regularly monitored and reviewed.

	▪ **Ongoing stewardship and policy sustainability:** Ongoing stewardship of the Action Plan is critical to ensure policy change is long-lasting and sustainable. In the USA, UK and many European countries, the sustainability of rare diseases policy is enshrined in legislation. **Theme #2: The need to prioritise the systematic building of knowledge, evidence and expertise** There is urgent need for the expansion of rare disease expertise and further development of evidence-based rare disease care. Systems must actively respond to existing evidence gaps. Processes that will build knowledge and evidence both quickly and sustainably must be prioritised. Clearer pathways through health and other systems are a necessity. Throughout the consultation process, stakeholders consistently raised the need for centres of excellence for rare diseases. Currently, rare disease clinics and research institutes with a focus on rare diseases are significantly under-resourced, and often work in isolation. To achieve real progress, existing strengths must be built upon to formalise a network of centres of excellence that is appropriate and accessible for all Australians. **Theme #3: The need for a person-centred approach and ongoing collaboration** To be successful, this Action Plan must progress meaningful involvement of people living with a rare disease across all areas. This includes ongoing collaboration and co-design with the many rare disease organisations that represent Australians living with a rare disease. These organisations enable connection and support, lead advocacy and awareness, and encourage active consumer participation. This Action Plan presents an important opportunity to embed the rare disease consumer voice in the design, implementation and evaluation of services for Australians at all levels. This has the potential to lead to better outcomes for people living with a rare disease as well as their families and carers. **Theme #4: The need to measure rare diseases** Limited data is a common feature in rare diseases. This is heightened by poor quality, disjointed collection methods and the ineffective use of data for rare diseases. Such limitations are evident across a range of areas, from health system classification to research. Research, monitoring and ongoing evaluation are critical in rare diseases because, ultimately, if we are not counting rare diseases, people living with rare diseases do not count. **Theme #5: The need for sustainable systems and workforce** Sustainable systems and workforce are critical to the long-term success of this Action Plan. Throughout stakeholder consultations, we heard many reports of staff shortages and a lack of funding. As such, there is a real need to build on, and invest in, the existing strengths of the workforce for rare diseases. National leadership is required to coordinate stakeholders to develop and implement a workforce strategy for rare diseases. The essential role of rare disease organisations must also be recognised and sustained. Rare disease organisations play a key role in raising disease awareness and providing much-needed person-centred information. These organisations often fill gaps in the system, not only in terms of awareness and education, but also in peer support and, increasingly, in the research and data sphere. However, these organisations are significantly under-resourced and are largely volunteer based, posing a risk to their long-term sustainability. **Theme #6: The need for stakeholder collaboration** The success of this Action Plan is underpinned by stakeholder involvement, collaboration and engagement. It is essential that all key stakeholders in the rare disease community, including people living with a rare disease, clinicians, researchers, governments and industry work together to progress this Action Plan.

	Theme #7: State, national and international partnerships as well as cross-sector collaboration Given the small populations and complexity involved in rare diseases, strong ongoing partnerships are invaluable. Global collaboration and the sharing of knowledge and expertise are often required to ensure the best outcomes for people living with a rare disease. Due to the nature of Australia's health and social systems, state and national partnerships are vital, as is the need for the ongoing facilitation of these partnerships. **Theme #8: The need to progress early implementation wherever possible** Rare diseases are often progressive and shorten life expectancy, and the burden of rare diseases remains unacceptably high. As such, implementation activities must build on successful initiatives already underway to address the need for urgency and to continue to build capacity, collaboration and coordination.
Governance and organisational structures	RVA (Rare Voices Australia) was commissioned by the Australian Government to develop the Action Plan on behalf of the rare disease sector. The Action Plan provides guidance and direction around key goals and priorities for Australians living with a rare disease. It sets out actions and activities, as determined by the sector, which could be introduced to improve the health and wellbeing of Australians living with a rare disease. The actions identified in the Action Plan are for consideration by a wide range of stakeholders, including governments at all levels, non-government organisations, the public and private health sectors, industry, researchers and academics, rare disease organisations and the wider community. The implementation of any of the actions outlined is a decision for each stakeholder, based upon their area of responsibility, governance remit, existing activities and future planning and directions in relation to rare diseases. **Implementation Mechanisms** A number of international exemplars of quality implementation mechanisms already exist. They include: ▪ The Genetic and Rare Diseases Information Center (USA) ▪ Rare Disease Centres of Excellence (UK) ▪ European Reference Networks (ERNs). Similar implementation mechanisms in Australia should be led by a national peak organisation that builds capacity in the rare disease sector. RVA is the current national peak organisation advocating for people living with a rare disease. Having demonstrated strong partnerships and linkages with the rare disease sector throughout its history, including in the development of the Action Plan, RVA is well positioned to lead its implementation in line with international exemplars. RVA is also best placed to build on, and utilise, existing relationships with international rare disease networks such as EURORDIS, IRDiRC and the more newly-developed Asia Pacific Alliance for Rare Disease Organisations (APARDO). It is critical that the national peak organisation (RVA) is resourced to raise the profile of rare diseases, both in Australia and internationally. RVA must also continue to collaborate with governments and the rare disease community to lead action for rare diseases. To cover the breadth of Australia, the national peak organisation would provide facilitator and secretariat support to: Centres of excellence located throughout Australia that act as localised points of contact. They may be comprised of research groups or institutes, clinics, hospitals and rare disease organisations. This mechanism builds on existing strengths in the sector, increasing its sustainability in the long-term. Further investment would respond to existing critical funding gaps and build workforce capacity, ensure person-centred collaboration and co-design, while allowing for specialisation and reducing duplication.

Funding model	Not mentioned. Funding gaps and recommendations for funding priorities noted in Actions 1.1.1, 2.2.2, 2.2.4, 2.3.2, 2.4.2, 2.4.3, 3.2.2, 3.2.3, 3.3.2 and 3.4.1.
	References and or links to relevant initiatives
Screening programmes (including newborn screening)	*See Action 1.1.3, 2.2.1, 2.2.2, 2.3.2.*
Personalised medicine, genomics, genetic counselling	*See Action 2.3.1, 2.4.1, 3.2.1.*
Models of care/care pathways	*See Action 1.1.2, 1.1.3, 1.3.2, 2.1.1, 2.1.2, 2.1.3, 2.2.1, 2.2.3, 2.2.4, 2.5.1.*
Workforce	*See Action 1.3.1, 1.3.2, 3.4.2, Theme #5.*
European Reference Networks	This Action Plan is comparable to other international rare disease plans and strategies, including those in Europe, the UK, Canada and the USA.
EU alignment and participation	*See Action 3.2.3, Theme #1, Theme #7. For international alignment, see Action 3.2.5.*
Health information (including rare disease registries)	*See Action 3.1.1, 3.1.2, 3.1.3, 3.1.4.*
Orphan medicines	*See Action 2.4.1, 2.4.2, 2.4.3.*
Rare disease research	*See Action 3.2.1, 3.2.2, 3.2.3, 3.2.4, 3.2.5, 3.3.1, 3.3.2, 3.4.1, 3.4.2.*
Alignment beyond the healthcare sector	*See Action 1.2.2, 2.5.2, 2.5.3, Theme #6.*

Any additional information (for example, background to the strategy or strategy development)	The National Strategic Action Plan for Rare Diseases is the first nationally coordinated effort to address rare diseases in Australia. The Action Plan aligns with, and expands on, the Call for a National Rare Disease Framework: 6 Strategic Priorities, which was published by RVA in June 2017. Additionally, it aligns with the National Strategic Framework for Chronic Conditions, the National Aboriginal and Torres Strait Islander Health Plan 2013–2023 and the WHO Global Action Plan for the Prevention and Control of Non communicable Diseases. Crucially, it also aligns with the Asia-Pacific Economic Cooperation (APEC) Action Plan on Rare Diseases.

Key: AIHW: Australian Institute of Health and Welfare; APEC: Asia-Pacific Economic Cooperation; APARDO: Asia Pacific Alliance for Rare Disease Organisations; CALD: Culturally and Linguistically Diverse; ERNs: European Reference Networks; EURORDIS: European Organisation for Rare Diseases; HTA: Health Technology Assessment; ICD-11: International Classification of Diseases 11th Revision; IRDiRC: International Rare Diseases Research Consortium; NBS: Newborn Bloodspot Screening; NCAR: Australian National Congenital Anomalies Register; NDIS: National Disability Insurance Scheme; OHTA: Office of Health Technology Assessment; RVA: Rare Voices Australia; SWAN: Syndrome Without A Name; UK: United Kingdom; USA: United States of America; WARDA: Western Australian Register of Developmental Anomalies; WHO: World Health Organization.

Table B2. Data extracted for Australia (Rare Voices Australia Status Report).

Australia	Strategy information
Author(s) **Title**	Rare Voices Australia (RVA) Implementing the National Strategic Action Plan for Rare Diseases: May 2023 Status Report[23]
Timeline	Activity scan conducted by RVA scan in September and October 2022 and during February 2023. Status Report published May 2023 – the first effort to track implementation of the Action Plan. (Action Plan launched in February 2020).
Overall aim(s)	**Objectives** 1. Track implementation of the Action Plan since its launch in 2020. 2. Identify projects, initiatives and achievements of various stakeholders and, where relevant, align these against the Pillars, Priorities and Themes in the Action Plan and map these to 5 key elements of progress in a logic model. 3. Identify gaps and strengths in Action Plan implementation to guide the sector towards the more effective and efficient use of time, expertise and resources. 4. Set a baseline for future monitoring and evaluation of Action Plan progress.
Themes and or priorities	**Pillars and Priorities as per the National Strategic Action Plan for Rare Diseases:** Pillar 1: Awareness and education Pillar 2: Care and support Pillar 3: Research and data. **Themes** (as per the Action Plan): Theme #1: The need for national leadership, coordination and consistency Theme #2: The need to prioritise the systematic building of knowledge, evidence and expertise Theme #3: The need for a person-centred approach and ongoing collaboration Theme #4: The need to measure rare diseases Theme #5: The need for sustainable systems and workforce Theme #6: The need for stakeholder collaboration Theme #7: State, national and international partnerships as well as cross-sector *(for example, specifically, across government sectors)* collaboration Theme #8: The need to progress early implementation wherever possible.
Targets (if specified) and measurement method(s) (where available)	*Not mentioned.*
Implementation action(s), lead(s) and key performance indicator(s)	**Mapping rare disease sector activities to Action Plan Pillars and Priorities** The activity scan captured over 380 activities from across the rare disease sector aligning with one or more Pillars and Priorities in the Action Plan. Some activities broadly addressed all rare diseases, while others related to a single rare disease, or an umbrella group of rare diseases. Activities were either at a national or jurisdictional level. The vast majority of activities were those undertaken by RVA Partner organisations (individual rare disease organisations). This is not surprising as this stakeholder group is the largest of those invited to contribute to this research, which included departments of health, clinicians and researchers, industry and peak bodies.

	…whilst each of these [pillars] is considered separately in the Action Plan, in reality, all Pillars are interrelated. As such, the strongest policy responses address priorities across multiple Pillars. Effective policy reform in one area will create change and momentum in other areas. Accordingly, activities that respond to multiple priorities and pillars should be prioritised. Number of activities per pillar and overlapping between pillars: ▪ Pillar 1: Awareness and education = 114 activities ▪ Pillar 2: Care and support = 150 activities ▪ Pillar 3: Research and data = 104 activities ▪ Pillars 1 and 2 = 18 activities ▪ Pillars 2 and 3 = 9 activities ▪ Pillars 1 and 3 = 7 activities ▪ Pillars 1, 2 and 3 = 3 activities. With most activities addressing Pillar 2: Care and Support and the majority being conducted by individual rare disease organisations, it is apparent that these organisations are taking on a number of care and support roles across the rare disease sector. In line with this observation, through RVA's mentorship and education program, RVA is aware of the significant burden on many rare disease organisations as they work to fill gaps in the care and support needs of patients and their families. **Tracking activities against 5 key elements of progress** Activities were grouped under five key elements of progress – logic model: 1. **Input**: Examples include funding and investment from various sources, sense of agency, people and relationships, and the contribution of time, specialised knowledge and skills. 2. **Activities or Processes**: What we do to transform input into output. For example, awareness campaigns, delivering education, research, pilot projects. 3. **Outputs**: Products of activity. For example, the number of people reached in an awareness campaign, resources, publications, frameworks, guidelines, new Models of Care. 4. **Outcomes**: Implementation of outputs. Short-term effects of outputs, including increased collaboration, changes in public/decision maker views and/or understanding. Embedding activity/guidelines/frameworks within systems and processes including care standards. 5. **Impact**: A measure of the difference our work is having on the health and wellbeing outcomes for Australians living with a rare disease. One example of an end goal is the systemic adoption of changes through policy reform. There is a consistent trend in the alignment of captured activities to the five key elements of progress across all three Action Plan Pillars, with most – regardless of the Pillar – in the Activity and Output stages and fewer in the later stages of Outcome and Impact. This points to similarities in sector progress in all areas of the Action Plan. Collectively, close to half the captured activities are in the 'Activities or Process' phase of the logic model, while only a fraction (approximately 5%) have reached the Impact phase. This is not unexpected three years into Action Plan implementation. Given the natural progression of the logic model continuum from Input through to Impact, the sector is likely to see many of the current Activities and Processes translate to Outputs, Outcomes and measurable Impact in the near future. **Tracking activities against Action Plan Themes**

	The majority of activities align with more than one Action Plan Theme, which meets the shared expectations of the sector. The greatest levels of activity alignment are across the following themes: ▪ Theme 1: National leadership, coordination and consistency ▪ Theme 2: Prioritisation of systematic building of knowledge, evidence and expertise ▪ Theme 3: A person-centred approach ▪ Theme 6: Stakeholder collaboration. By comparison**,** fewer activities align with: ▪ Theme 4: Rare disease measurement ▪ Theme 5: Sustainable systems and workforce ▪ Theme 7: State, national and international cross-sector (i.e. specifically across government sectors) collaboration ▪ Theme 8: Progression of early implementation wherever possible. These data also speak to the relationships between the Action Plan Themes and Pillars across all captured activities. Some Pillars are inherently aligned with particular themes; however, there are some themes requiring more attention in specific Pillars. Unsurprisingly, most activities aligning with Theme 4: 'Rare disease measurement' fall under Pillar 3: Research and Data. For Theme 5: 'Sustainable systems and workforce' and Theme 8: 'Progression of early implementation wherever possible', Pillar 2: Care and Support activities are most prominent, pointing to greater levels of progress in the activities under this Pillar compared to other Action Plan Pillars. In the next phase of Action Plan implementation, it is important to prioritise the measurement of rare diseases through coordinated data collection, and the development of sustainable systems and workforce, which are identified across the Action Plan in the critical enablers, priorities and actions as well as the Action Plan Themes. The sector also needs to think of ways to work more collaboratively across government sectors, jurisdictions and internationally, and push for early implementation wherever possible. The need for 'rare disease care and support that is integrated, incorporating clear pathways throughout health, disability and other systems' (Action 2.1.1) is highlighted under Pillar 2: Care and Support and is becoming increasingly prioritised in some jurisdictions working to connect people living with a rare disease to all areas of government support. It is vital that this work is extended to all jurisdictions across the country. Of note, fewer than 20 captured activities appear to address priority populations outlined in the more granular implementation steps of the Action Plan. Future measurements of Action Plan implementation should include specific questions around how individual activities have considered the needs of these priority populations to allow stronger conclusions to be drawn about progress in these areas.
Governance and organisational structures	Implementation of the Action Plan is the ongoing responsibility of all stakeholders, including all levels of government, the public and private health sectors, rare disease organisations, industry, researchers and the wider community. RVA remains committed to leading the collaborative implementation of the Action Plan and will continue to monitor and evaluate progress and steer the sector to the realisation of the collective vision for the best possible health and wellbeing outcomes for Australians living with a rare disease.
Funding model	**Information provided by email from key representative in Australian Government Department of Health and Aged Care on 26 November 2023:** "Funding of $4.03 million over four years from 2020-21 is being provided for implementation activities that align with the Action Plan. Of this funding, $1 million is being provided for rare disease awareness and education activities. The remaining $3.03 million is being provided to undertake development and delivery of education resources for health professionals, and activities to support people living with a rare disease." **Maintaining momentum: Things to consider for sustainable and systemic change**

	All governments must urgently invest in the rare disease sector. To drive systemic change, investments should leverage and build on existing expertise, knowledge, resources and infrastructure. Learnings from this activity scan also highlight the need to invest in regular reviews of Action Plan progress to support iterative implementation plans for a responsive, dynamic, transformative and targeted approach.
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including new-born screening)	*Activities included under Theme 1 and Theme 8.*
Personalised medicine, genomics, genetic counselling	*Activities included under Theme 1 and Theme 8 (for example, Mitochondrial Donation Law Reform (Maeve's Law) Act 2022).*
Models of care/care pathways	*Activities included under Theme 1 and Theme 2.*
Workforce	*Activities included under Theme 2, Theme 5, Theme 6 and Theme 8.*
European Reference Networks	*Not mentioned. Need for networks of Centres of Excellence/Expertise noted under Theme 1 and Theme 2.*
EU alignment and participation	*Not mentioned. Need for global collaboration noted under Theme 7.*
Health information (including rare disease registries)	*Activities included under Theme 2, Theme 4 and Theme 8.*
Orphan medicines	*Not mentioned.*
Rare disease research	*Activities included under Theme 1, Theme 2, Theme 4 and Theme 6.*
Alignment beyond the healthcare sector	*Activities included under Theme 3, Theme 6 and Theme 7.*
Any additional information (for example, background to the strategy or strategy development)	**Maintaining momentum: Things to consider for sustainable and systemic change** This initial, more comprehensive, approach to mapping progress has enabled clarification of RVA's methods for measuring Action Plan implementation progress. It has led to the establishment of a baseline for more streamlined and targeted monitoring, evaluation and reporting on implementation progress. This baseline will be used in future evaluations to track implementation trajectory over time. However, it should be acknowledged that without verified indicators or metrics to assess and track progress across the rare disease sector, measuring impact can be subjective, particularly given the varied connotations of impact at an individual level compared to a sector-wide level. Person-centred, verified indicators or metrics are needed to facilitate objective measurements of impact in rare disease.

	Future efforts to monitor and evaluate Action Plan progress should be refined to increase the sample of captured activities through improved data collection methods. In addition, data analysis and reporting should be streamlined to enable the sharing of simple progress snapshots over time. This work requires ongoing commitment of the rare disease sector to track Action Plan progress, and to iterative monitoring, evaluation and refinement of individual activities to meet intended outcomes.

Key: RVA: Rare Voices Australia.

Table B3. Data extracted for Austria (National Action Plan Full Text)

Austria	Strategy information
Author(s) **Title**	Austrian Federal Ministry of Health (*Bundesministerium für Gesundheit*, BMG) and Austrian National Public Health Institute (*Gesundheit Österreich GmbH*, GÖG) National Action Plan for Rare Diseases (NAP.se)[47]
Timeline	2014-2018
Overall aim(s)	To improve the lives of Austrian patients affected by rare diseases regardless of gender, age, degree of disability or socio-economic status, as well as their families and extended social and professional environment. The Plan intended to define appropriate measures and incentives to overcome existing fragmentation, improve the flow of information, optimise and coordinate processes and eliminate points of weakness. The Plan combines plan and strategy.
Themes and or priorities	Nine thematic priorities (fields of action) which take account of both national requirements and European recommendations: 1. Mapping/illustrating rare diseases in the health and social system. 2. Improving medical-clinical care for those affected by rare diseases. 3. Improving the diagnosis of rare diseases. 4. Improving therapy and access to therapies for rare diseases. 5. Promoting research in the area of rare diseases. 6. Improving knowledge and awareness of rare diseases. 7. Improving epidemiological knowledge in the context of rare diseases. 8. Establishment of permanent advisory committees for rare diseases at the BMG (Federal Ministry of Health). 9. Acknowledgement of the merits of patient organisations for rare diseases. The fields of action are derived from the following considerations: ▪ Improved, nationally consistent access to diagnosis, treatment, rehabilitation and care thanks to transparent treatment paths ▪ Rapid, quality-assured diagnosis and care in defined expertise centres and laboratories with the participation of all levels of care in order to ensure the best possible, quick and local care ▪ Secured comprehensive medical care for people with rare diseases through long-term care ensured financing of therapies for rare disease (including from orphan drugs) ▪ Statistical recording of the frequencies of the individual rare diseases in Austria using suitable documentation and ensuring adequate compensation for the treatment of rare disease based on this documentation ▪ Comprehensive awareness of rare diseases and the associated treatment options particularly in the health professions involved ▪ Strong independent self-help groups, which are not only essential for a higher quality of life, but also contribute enormously to the general care of sick people.
Targets (if specified) and measurement method(s) (where available)	Goals listed for each field of action (in bold): **1. Mapping/illustrating rare diseases in the health and social system** ▪ Goal 1: Introduction of suitable documentation (coding) for rare diseases in all expertise centres and subsequently optional extension to other care levels. ▪ Goal 2: Ensure adequate compensation for medical services for rare diseases. ▪ Goal 3: Introduction of a personal information card for patients with rare diseases.

	2. Improving medical and clinical care for those affected by rare diseases *A. Designation of specialised centres for groups of rare diseases* ▪ Goal 1: Summary of the individual rare diseases into medically meaningful disease groups on the basis of common clinical, differential diagnostic and therapeutic and or pathophysiological characteristics as well as definition of the interdisciplinary and multiprofessional requirements in the (medical and social) care of people with diseases in these groups. ▪ Goal 2: Designation of specialised centres for defined groups of rare diseases, which are divided into three levels of care in terms of their requirements profile and range of services. ▪ Goal 3: Integration of these specialised centres into the Austrian care landscape through intensified networking of everyone involved. ▪ Goal 4: Providing framework conditions for the integration of Austrian expertise into European Reference Networks (ERNs). *B. Establishment of a national coordination centre for rare diseases* NKSE established in 2011. Its goals: ▪ Goal 1: Identify deficits regarding rare diseases in the health and care system. ▪ Goal 2: Develop a national strategy to address the identified deficits in the rare diseases sector (NAP.se). ▪ Goal 3: Support the implementation of the National Action Plan for Rare Diseases (NAP.se). ▪ Goal 4: Survey and structuring of the range of medical services in the area of rare diseases. ▪ Goal 5: Promote uniform access to medical care for rare diseases across Austria including therapies at the 'best point of service'. ▪ Goal 6: Information hub for rare diseases. ▪ Goal 7: Networking at European level to ensure continuous exchange in the area of rare diseases. *C. Establishment and sustainable support of a comprehensive information system for rare diseases (Orphanet)* ▪ Goal 1: Expansion of the contents of the database and ensuring long-term financing for Orphanet Austria. **3. Improving the diagnosis of rare diseases** ▪ Goal 1: Development and implementation of quality and performance criteria for diagnostic laboratories for rare diseases. ▪ Goal 2: Designation of specialised laboratories for rare diseases and or groups of rare diseases. ▪ Goal 3: Integration of these specialised laboratories into the Austrian healthcare landscape through close networking of all healthcare levels involved. ▪ Goal 4: Development of financing models for laboratory diagnostic services for rare diseases. ▪ Goal 5: Development and implementation of uniform Austria-wide standards for instrumental diagnostics in rare diseases. ▪ Goal 6: Designation of specialised diagnostic facilities for rare diseases and or groups of rare diseases in accordance with the aforementioned Austria-wide standards. ▪ Goal 7: Establishment of an official scientific advisory board at ministerial level for the Austrian newborn screening program. ▪ Goal 8: Development of an Austrian 'Undiagnosed Diseases Programme'. **4. Improving therapy and access to therapies for rare diseases** ▪ Goal 1: Networking at European level to ensure sustainable financing of orphan drugs in the long term. ▪ Goal 2: Determine the costs of selected drugs without overlapping indications for the treatment of people with rare diseases in both general practice and institutional settings. ▪ Goal 3: Ensuring consistent access to therapies at the best point of service. ▪ Goal 4: Creation of a nationwide uniform catalogue of services for selected remedies (pilot project for rare diseases).

	▪ Goal 5: Ensure continuous access to adequate medical care. **5. Promoting research in the area of rare diseases** ▪ Goal 1: Make visible and create awareness of existing national and international funding opportunities for rare diseases in the scientific community. ▪ Goal 2: Creating structural framework conditions to ensure high-quality applications (linked to field of action 2A, goal 2). ▪ Goal 3: Networking domestic and other European centres of expertise in order to participate together in international funding programmes. ▪ Goal 4: Coordination of support for rare disease-specific research initiatives in order to position Austria as a research location in the field of rare diseases. **6. Improving knowledge and awareness of rare diseases** ▪ Goal 1: Expansion of the level of knowledge of the most important sources of information (especially in primary care: doctors and other health professionals). ▪ Goal 2: Strengthening patient safety and health literacy through objective, quality-assured and target group-specific information and thereby promoting access to services and service provision at the "best point of service" (better guidance through the system or signposts). ▪ Goal 3: Increase awareness of rare diseases in all target groups and raise awareness of the topic. **7. Improving epidemiological knowledge in the context of rare diseases** ▪ Goal 1: Establishment of a comprehensive, quality-assured epidemiological recording system for rare disease patients in Austria. ▪ Goal 2: Consideration of interoperability with existing systems at national and European levels. ▪ Goal 3: Coordination with current and future developments at European level. **8. Establishment of permanent advisory committees for rare diseases in the Federal Ministry of Health** ▪ Goal 1: Permanent establishment of both committees (the Expert Group for Rare Diseases and the Strategic Platform for Rare Diseases). ▪ Goal 2: National Advisory Council for Rare Diseases: continuous provision of expert knowledge or knowledge from research and practice on rare diseases. ▪ Goal 3: Strategic platform for rare diseases: strategic support of the NKSE work. **9. Recognition of the achievements/services/benefits of support groups.** ▪ Goal 1: To ensure Austria-wide representation for people with rare diseases, including as a contact person for people with diseases for whom there is no separate self-help organisation and or self-help group. ▪ Goal 2: Clarification of the role of self-help, promotion of independence and transparency with the aim of ensuring long-term financing. ▪ Goal 3: Recognition of the expertise and experiences of people with rare diseases and those of their relatives and creation of participatory decision-making structures. ▪ Goal 4: Survey the health economic effects of self-help. ▪ Goal 5: Strengthen the image of self-help among the public.

Implementation action(s), lead(s) and key performance indicator(s)	Implementation of the Plan and its success to be monitored using specific indicators for each field of action, in line with European developments and procedures, which are still to be determined. The creation of the indicators is scheduled to be completed in 2015. Eighty-two actions listed according to the relevant field of action (in bold) and associated goal: **Priority 1: Mapping/illustrating rare diseases in the health and social system** Goal 1: Introduction of suitable documentation (coding) in all expertise centres and subsequently optional extension to other care levels. 1. Collaboration in the development of a coding system for rare diseases. a) Organising a workshop on coding with national and German participants. *Responsible*: BMG/NKSE. *Schedule*: 2014. b) Follow-up steps will be defined after the workshop. *Responsible*: BMG. *Schedule*: to be determined following a). 2. Introduction of suitable coding documentation in expertise centres (Type A, Type B, Type C). *Responsible*: BMG; NKSE; hospital providers; federal states. *Schedule*: following Action 1 and depending on the concrete designation of appropriate centres of expertise. 3. Examining the possible expansion of the coding documentation to areas outside the expertise centres (other hospitals, private practice areas). *Responsible*: BMG; SV; federal states. *Schedule*: following Action 2. Goal 2: ensuring adequate compensation for medical services. 4. Check whether the current billing and remuneration catalogues sufficiently reflects the service activities in connection with rare diseases. *Responsible*: BMG; NKSE; SV; federal states. *Schedule*: following Action 2. 5. Depending on the result of action 4, adapt the corresponding billing and remuneration catalogues to ensure adequate compensation for the treatment of rare diseases in all areas of care. *Responsible*: BMG; SV; federal states. *Schedule*: following Action 4. Goal 3: Introduction of a personal information card. 6. Create a concept for introducing a patient information card. *Responsible*: BMG/NKSE; Pro Rare Austria. *Schedule*: 2016. 7. Consecutive: Development of an online platform for treatment and emergency guidelines for defined groups of rare diseases. *Responsible*: Orphanet in collaboration with medical specialist societies; Quality specialist group. *Schedule*: following Action 6. **Priority 2: Improving medical and clinical care for those affected by rare diseases** *A. Designation of specialised centres* Goal 1: Summary of the individual rare diseases into medically meaningful disease groups. 8. Continue and complete work on grouping rare diseases (combining the individual diseases into medically sensible groups). *Responsible*: BMG/NKSE; medical professional societies. *Schedule*: 2014. 9. Continuing and completing the work on assigning the individual rare diseases to (primarily responsible) organ or cross-sectional subjects. *Responsible*: BMG/NKSE; medical professional societies. *Schedule*: 2014. 10. Continue and complete the collection of interdisciplinary and multi-professional requirements for individual rare diseases and or groups of RDs.

	Responsible: BMG/NKSE; medical professional societies; Planning specialist group; Quality specialist group; hospital providers. *Schedule*: 2014/2015. 11. Regular review/update of RD grouping as well as the definition of interdisciplinary and multi-professional requirements for RD/groups of RDs. *Responsible*: BMG/NKSE; medical professional societies; Planning specialist group; Quality specialist group; hospital providers. *Schedule*: 2015 ff. 12. Public information on the grouping of rare diseases (for example, website); see also Action 19). *Responsible*: BMG/NKSE. *Schedule*: 2015 ff. Goal 2: Designation of specialised centres for defined groups which are divided into three levels of care. 13. Anchoring the general performance and quality criteria for Type A, B and C centres in a suitable planning instrument. *Responsible*: NKSE/GÖG; Planning specialist group; hospital providers; Federal Health Commission (BGK). *Schedule*: 2014/2015. 14. Develop specific performance and quality criteria for Type B and consecutive Type C centres for specified groups of rare diseases, anchoring the criteria in a suitable planning instrument. *Responsible*: NKSE; expert group for rare diseases; responsible specialist groups; hospital providers. *Schedule*: 2014 ff. 15. Development of an application, assessment and designation process for Types A, B and C centres: coordinating with corresponding procedures at EU level. *Responsible*: NKSE (partially in collaboration with selected pilot Type B centres); coordination with BMG, Main Association of Austrian Social Insurance Institutions (HVB), federal states, hospital; authorities. *Schedule*: 2015. 16. Definition of a coordinating body for the technical administration of the application process (see also Action 17). *Responsible*: BMG; HVB; Planning specialist group. *Schedule*: 2015. 17. Carrying out (top-down and bottom-up) application rounds and designation of Type B, Type C and consecutive Type A centres. *Responsible*: NKSE or other coordinating body; designation office. *Schedule*: 2015 ff. 18. Public information about the designated centres (for example, website). *Responsible*: BMG/NKSE; designation office. *Schedule*: following designations. 19. Workshop to develop indicators for measuring the quality of patient care and to develop procedures for corresponding outcome measurements; coordination with comparable processes at EU level. *Responsible*: BMG/NKSE; Quality specialist group; Planning specialist group. *Schedule*: 2016. 20. Development of a separate evaluation and audit procedure for the reviews of the services already designated Type A and B centres at five-year intervals and coordination with corresponding processes at EU level. *Responsible*: BMG/NKSE; if necessary, additional coordinating body; designation office. *Schedule*: 2016/2017. Goal 3: Integration of these specialised centres through intensified networking. 21. Supporting horizontal and trans-sectoral networking of Types A, B and C centres with other care levels. *Responsible*: BMG/NKSE. *Schedule*: following Action 17. Goal 4: Providing framework conditions for the integration of Austrian expertise into ERNs. 22. Support for European networking with ERNs. *Responsible*: BMG/NKSE. *Schedule*: 2015 ff. *B. Establishment of a national coordination office for rare diseases* Goal 1: Identify deficits regarding rare diseases in the health and care system. 23. Assessing the care needs of patients with rare diseases in Austria.

	Responsible: BMG/NKSE. *Schedule*: completed in 2012. Goal 2: Develop a national strategy to address the identified deficits in the area of rare diseases (NAP.se). 24. Creating a National Action Plan for Rare Diseases. *Responsible*: BMG/NKSE. *Schedule*: 2013/2014 (publication 2015). Goal 3: Support the implementation of the National Action Plan for Rare Diseases (NAP.se). Goal 4: Collection and structuring of the medical service offering in the area of rare diseases. Goal 5: Promote uniform access to medical care for rare diseases across Austria including therapies at the 'best point of service'. 25. Supporting the implementation process of the NAP.se. *Responsible*: BMG/NKSE. *Schedule*: 2014-2018. Goal 6: Information hub for rare diseases. 26. Providing relevant information on rare diseases for selected target groups. *Responsible*: BMG/NKSE. *Schedule*: constantly. Goal 7: Networking at European level to ensure continuous exchange in the area of rare diseases. 27. Participate in meetings of European commission bodies in the context of rare diseases. Optional: collaboration on European projects related to rare diseases. *Responsible*: BMG/NKSE. *Schedule*: constantly. *C. Continue and sustainably secure Orphanet as a comprehensive information system for rare diseases.* Goal 1: expansion of the contents of the database and ensuring long-term financing for Orphanet Austria. 28. Developing a concept for long-term financing for Orphanet Austria. *Responsible*: BMG/NKSE; Federal Ministry of Science, Research and Economy (BMWFW); federal states; HVB/SV; if necessary, other financiers. *Schedule*: 2014/2015. 29. Completion and continuation of the Orphanet database and consideration of the Orphanet quality scheme. *Responsible*: Orphanet Austria. *Schedule*: 2014 ff. **Priority 3: Improving the diagnosis of rare diseases** Goal 1: Development and implementation of quality and performance criteria for diagnostic laboratories for rare diseases. 30. Continue and complete the definition of performance and quality criteria for medical laboratories involved in the diagnosis of rare diseases. *Responsible*: BMG/NKSE; experts (selected members of the advisory board for rare diseases (see priority 8) as well as external experts). *Schedule*: 2015 ff. 31. Defining requirements for the competence of professionals involved in the diagnosis of rare diseases. *Responsible*: BMG/NKSE; experts (as per Action 30); Quality specialist group. *Schedule*: 2015 ff. Goal 2: Designations of Specialised laboratories for rare diseases or groups of rare diseases. 32. Developing an application, assessment and designation process for medical laboratories involved in the diagnosis of rare diseases. *Responsible*: BMG/NKSE; coordination with HVB; federal states. *Schedule*: following Goal 1. 33. Implementing the designation (establishing a designation office). *Responsible*: BMG/NKSE; coordination with HVB; federal states. *Schedule*: following Action 32. 34. Setting up an official website to make designated laboratories visible. *Responsible*: BMG/NKSE; designation office. *Schedule*: following Action 33.

	35. Develop an evaluation and audit process for designated laboratories. *Responsible*: BMG/NKSE; if necessary, additional coordinating body; Quality specialist group; designation office. *Schedule*: following Action 33. Goal 3: Integration of these specialised laboratories into the Austrian healthcare landscape through close networking of all healthcare levels involved. 36. Supporting the nationwide networking of designated laboratories with each other and with other levels of care; Support in networking with Orphanet. *Responsible*: NKSE; Orphanet Austria. *Schedule*: expected to be relevant from 2018. Goal 4: Development of financing models for laboratory diagnostic services for rare diseases. 37. Examination and possible revision of the relevant service catalogues. *Responsible*: Payer. *Schedule*: expected to be relevant from 2018. Goal 5: Development and implementation of uniform Austria-wide standards for instrumental diagnostics. Goal 6: Designation of specialised diagnostic facilities in accordance with the aforementioned Austria-wide standards. 38. Developing competency criteria for experts, who are involved in the diagnostics of rare diseases. *Responsible*: BMG/NKSE; experts; Quality specialist group. *Schedule*: expected to be relevant from 2018. Goal 7: Establishment of an official scientific advisory board at ministerial level for the Austrian newborn screening programme. 39. Setting up a permanent scientific advisory board for the Austrian newborn screening. *Responsible*: BMG and BMWFW. *Schedule*: 2015. Goal 8: Development of an Austrian "Undiagnosed Diseases Programme". 40. Development of a concept for an Undiagnosed Diseases Programme in Austria. *Responsible*: BMG/NKSE; experts. *Schedule*: 2016. **Priority 4: Improving therapy and access to therapies for those affected by rare diseases.** Goal 1: Networking at the European level to ensure sustainable financing of orphan drugs. 41. Participation in European cooperation projects to secure sustainable financing of orphan drugs, such as Mechanisms of Coordinated Access to Orphan Medicinal Products in Europe (MoCA-OMP). *Responsible*: HVB; BMG; industry; support from NKSE. *Schedule*: 2014 ff. Goal 2: Determine the costs of selected drugs without overlapping indications for the treatment of people with rare diseases in both general practice and institutional settings. 42. Price collection of selected orphan drugs in institutional and community-based sectors (including purchasing modalities such as joint purchasing and possible managed entry agreements). *Responsible*: NKSE/GÖG; HVB; hospital pharmacies; legal entity representatives of state hospitals; industry. *Schedule*: 2014/2015. 43. Providing expertise on rare diseases for the Medicines Commission (if required). *Responsible*: GÖG. *Schedule*: if necessary. 44. Co-developing concept proposals for the Medicines Commission for an improved financing strategy for selected high-priced orphan drugs (if required). *Responsible*: NKSE/GÖG. *Schedule*: if necessary. Goal 3: Ensuring consistent access to therapies at the best point of service. 45. Establishing optimised supply processes at the respective "best point of service". *Responsible*: BMG; federal states; HVB; NKSE/GÖG. *Schedule*: 2016 ff.

	46. Developing measures to minimise problems in the area of therapies for rare diseases. *Responsible*: Pro Rare Austria; BMG/NKSE. *Schedule*: 2014 ff. Goal 4: Creation of a nationwide uniform catalogue of services for selected remedies (pilot project for rare diseases). 47. Establishing a discussion group to introduce a uniform service catalogue for medical devices (pilot project for rare diseases). *Responsible*: HVB; BMG; federal states; support from NKSE. *Schedule*: 2015. Goal 5: Ensure continuous access to adequate medication care. 48. Establishing a regular exchange between chief physicians, social health insurance and patient representatives. *Responsible*: Pro Rare Austria; HVB. *Schedule*: constantly. 49. Development of a cross-agency, uniform catalogue of criteria (for example, in the form of a checklist) for the approval of orphan drugs and medical devices in the area of rare diseases as a support instrument for social insurance carriers in decision-making in the context of individually assessed medical decisions on a case-by-case basis. *Responsible*: HVB; support from NKSE. *Schedule*: 2015 ff. **Priority 5: Promoting research in the field of rare diseases.** Goal 1: Make visible and create awareness of existing national and international funding opportunities for rare diseases in the "scientific community". 50. Providing specific information/links for rare disease relevant tenders on the NKSE website in cooperation with the relevant funding agencies and institutions. *Responsible*: NKSE as an information hub; BMWFW. *Schedule*: 2014 ff. 51. Targeted information about coaching workshops offered by funding institutions to support applications. *Responsible*: NKSE as an information hub. *Schedule*: 2015 ff. Goal 2: Creation of structural framework conditions to ensure high-quality applications (linked to Priority 2, designation of specialised centres). 52. Designation of expertise centres with a focus on research. *Responsible*: Expertise centres and expertise clusters (optionally also associated centres); hospital providers; if applicable, university management; NKSE as an information hub. *Schedule*: 2015 ff. Goal 3: Networking domestic and other European centres of expertise in order to participate together in international funding programmes. 53. Austria's participation in ERN regarding research aspects. *Responsible*: Expertise centres and cluster model; NKSE as an information hub. *Schedule*: expected to be relevant from 2016. Goal 4: Coordination of support for rare disease-specific research initiatives in order to position Austria as a research location in the field of rare diseases. 54. Dialogue with the relevant stakeholders, especially with funding agencies and rare disease-relevant research institutions. *Responsible*: BMWFW; NKSE as an information hub. *Schedule*: 2014 ff. **Priority 6: Improving knowledge and awareness of rare diseases.** Goal 1: Expansion of the level of knowledge of the most important sources of information. 55. Imparting basic knowledge about rare diseases and the possible options associated with it, treatment options. *Responsible*: health service providers; professional associations; BMG/NKSE; Pro Rare Austria. *Schedule*: 2014 ff. 56. Specific quality-assured further education and training measures for doctors, including integration of topics on rare diseases into the ÖÄK's advanced training programme, presentations on the topic at specialist conferences, development of e-learning concepts.

	Responsible: Austrian Medical Association (ÖÄK); BMG/NKSE; Centres of Expertise. *Schedule*: 2014 ff. 57. Specific quality-assured further education and training measures for other health professions. *Responsible*: professional groups; Centres of Expertise; BMG. *Schedule*: 2014 ff. 58. Information for relevant authorities in the health and social sector. *Responsible*: BMG/NKSE. *Schedule*: 2015 ff. 59. Central and clear presentation of further training courses on rare diseases. *Responsible*: ÖÄK; professional groups; BMG/NKSE. *Schedule*: 2014 ff. Goal 2: Strengthening patient safety and health literacy through objective, quality-assured and target group-specific information. 60. Adding a focus on rare diseases in the health portal. *Responsible*: GÖG health portal; support from NKSE. *Schedule*: 2014 ff. See Action 29: Providing quality-assured information on rare diseases. *Responsible*: Orphanet Austria. *Schedule*: 2014 ff. Goal 3: Increase awareness of rare diseases in all target groups and raise awareness of the topic. 61. Definition of specific contact persons (person/department) for interest groups in the area of rare diseases. *Responsible*: all relevant system partners. *Schedule*: since 2011; Founding of NKSE, founding of Pro Rare Austria. 62. Promote networking and dissemination of knowledge. *Responsible*: expert group for rare diseases; strategic platform for rare diseases. *Schedule*: constantly. 63. Public relations. *Responsible*: all system partners; media. *Schedule*: constantly. **Priority 7: Improving epidemiological knowledge in the context of rare diseases.** Goal 1: Establishment of a comprehensive, quality-assured epidemiological recording system for patients with rare diseases. 64. Inventory of existing patient registers for rare diseases and, if necessary, other relevant data collection systems in Austria. *Responsible*: Orphanet Austria; NKSE; Pro Rare Austria. *Schedule*: 2015 ff. 65. Definition and coordination of (data protection) legal, structural and financial framework conditions and provisions for quality assurance. *Responsible*: BMG/NKSE; hospital providers. *Schedule*: 2015 ff. Goal 2: Consideration of interoperability with existing systems at national and European levels. 66. Ensuring interoperability with existing relevant national and international patient registries and data collection systems. *Responsible*: BMG/NKSE; federal states; SV; hospital providers. *Schedule*: as part of the definition and voting process. Goal 3: Coordination with current and future developments at European level. 67. Developing a minimum data set with international developments in mind. *Responsible*: BMG/NKSE; hospital providers. *Schedule*: 2014 ff. 68. Setting up an epidemiological platform for quality assurance and coordination (building on the results of previous actions). *Responsible*: BMG/NKSE; Planning specialist group; hospital providers. *Schedule*: following the previous actions. **Priority 8: Establishment of permanent advisory committees for rare diseases at the BMG.** Goal 1: Establish both committees. 69. Constituting the new "Rare Advisory Board" to replace the expert group for rare diseases as an advisory board in accordance with Section 8 of the Federal Ministries Act.

	Responsible: BMG. *Schedule*: 2014. 70. Maintaining the Strategic Platform for Rare Diseases. *Responsible*: BMG. *Schedule*: 2014. Goal 2: National Advisory Council for Rare Diseases – continuous provision of expert knowledge from research and practice. 71. Participation in meetings of the Advisory Board for Rare Diseases and advisory role in the implementation of the NAP.se and other issues in the context of rare diseases. *Responsible*: BMG/NKSE; members of the Advisory Board for Rare Diseases. *Schedule*: 2014-2016 ff. 72. Dissemination of information and recommendations from the Advisory Board for Rare Diseases in the respective institutions and interest groups. *Responsible*: BMG/NKSE; members of the Advisory Board for Rare Diseases. *Schedule*: 2014-2016 ff. Goal 3: Strategic Platform for Rare Diseases – strategic support of NKSE work. 73. Participation in meetings of the Strategic Platform for Rare Diseases. *Responsible*: BMG/NKSE; Strategic Platform for Rare Diseases. *Schedule*: 2014-2016 ff. 74. Strategic support in the implementation of the NAP.se and other issues in the context of rare diseases. *Responsible*: BMG/NKSE; Strategic Platform for Rare Diseases. *Schedule*: 2014-2016 ff. **Priority 9: Recognition of self-help achievements.** Goal 1: Ensure Austria-wide representation for people with rare diseases. 75. Establishment of an Austria-wide umbrella organisation of self-help groups for people with rare diseases. *Responsible*: Pro Rare Austria. *Schedule*: founding of Pro Rare Austria in December 2011. Goal 2: Clarification of the role of self-help, promotion of independence and transparency with the aim of ensuring long-term financing. 76. Creating framework conditions to ensure long-term financing. *Responsible*: financiers; legislature (BMG); ARGE self-help; Pro Rare Austria. *Schedule*: 2014 ff. 77. Definition of quality criteria (minimum standards) for financing self-help organisations. *Responsible*: ARGE self-help; Pro Rare Austria; payers (for example, federal government, federal states and HVB). *Schedule*: constantly. 78. Clarification of the legitimacy for the collective representation of patient interests (in coordination with other relevant patient organisations such as the patient advocacy group). *Responsible*: BMG; ARGE self-help; patient advocacy. *Schedule*: 2014 ff. 79. Non-material and structural support for self-help (for example, premises, training courses, etc.). *Responsible*: all system partners; GÖG (rooms are already made available). *Schedule*: constantly. Goal 3: Recognition of the expertise and experiences of people with rare diseases and those of their relatives and creation of participatory decision-making structures. 80. Representation of self-help for rare diseases in decision-making bodies and inclusion in decision-making processes. *Responsible*: all system partners; ARGE self-help; Pro Rare Austria. *Schedule*: Pro Rare Austria has been represented in the Expert Group for rare diseases of the BMG since 2011. Goal 4: Survey the health economic effects of self-help. 81. Initiating scientific studies to demonstrate the health economic effects of self-help. *Responsible*: relevant research institutions; Pro Rare Austria. *Schedule*: 2014 ff. Goal 5: Strengthen the image of self-help among the public.

	82. Public relations: for example, contributions in media, events, public recognition. *Responsible*: all system partners; BMG/NKSE; Pro Rare Austria; media. *Schedule*: 2014 ff.
Governance and organisational structures	**Priority 8: Establishment of permanent advisory committees for rare diseases in BMG.** ***National context*** By setting up two advisory committees, the Expert Group for Rare Diseases and the Strategic Platform for Rare Diseases, the BMG pursued the goal of incorporating knowledge and expertise on rare diseases from research and lived practice into the work of the NKSE. When creating the NAP, the committees had or generally have different, complementary mandates. The Expert Group had the specific task of supporting the NKSE through critical reflection and discussion of the NKSE concepts as well as through providing advisory support for submitting your own suggestions. The Strategic Platform, on the other hand, was primarily tasked with examining the feasibility of the concepts developed by the NKSE in collaboration with the Expert Group. Expert Group for Rare Diseases The term of office of the Expert Group extended from January 2011 to December 2013. It replaced the OSR's rare diseases sub commission, which ended in December 2010, and carried out its work within the framework of the mandate described above as a pure advisory body without binding decision-making authority. In comparison to the previous sub commission, the expert group was expanded to include several actors (Ministry of Science, federal states, hospital authorities) and was composed of representatives of the following institutions and areas: BMG Section III; HVB; medical specialists for rare diseases (including selective screening/newborn screening); Ministry of Social Affairs; Ministry of Science; federal states; hospital providers; Austrian Medical Association; PHARMIG – Association of the Austrian Pharmaceutical Industry; medical law and medical ethics sectors; AGES/PharMed; Orphanet; NKSE/GÖG; two vacant places if required. In 2014, the Expert Group for Rare Diseases will be replaced by an "Advisory Board for Rare Diseases" (according to Section 8 of the Federal Ministry Act). Strategic Platform for Rare Diseases In contrast to the Expert Group, the Strategic Platform was set up from the outset as a permanent committee with a strategic support and feedback function between the BMG, the federal states and the social insurance providers. In contrast to the Expert Group, it has extensive decision-making authority on the content developed by the NKSE, which is only limited by the decision-making authority of those institutions, committees and specialist groups in the healthcare system that are separately and ultimately responsible for a specific topic. The strategic platform is made up of representatives from the following institutions: BMG Sections I and III; federal states; HVB; GÖG. *See Actions 69-74.*
Funding model	The central financiers in the healthcare system (federal, state, social insurance) were involved in the entire process of creating the NAP.se. The implementation of measures is associated with costs. These must be taken into account when planning by the actors involved. However, there is currently no defined budget available; budget frameworks set for several years may also need to be taken into account. The actual costs for each individual measure proposed in NAP.se are determined during the concrete planning and definition of the respective implementation process - analogous to the development of indicators. The institutions involved in the implementation are promptly included in the cost estimate so that the potential financiers can plan the required budget accordingly. At the end of the term of the current NAP.se (2018), the health ministry, with the support of the NKSE, will provide a summary of the total funds used for the development and implementation of the NAP.se.

	Priority 5: Promoting research in the area of rare diseases List of funding institutions: ▪ Fund for the Promotion of Scientific Research (FWF) ▪ Austrian Research Promotion Agency (Österreichische Forschungsfördergesellschaft mbH, FFG) ▪ Austrian Business Services Society (Austria Wirtschaftsservice Gesellschaft mbH, AWS) ▪ Anniversary Fund of the Austrian National Bank ▪ Federal state-specific funds.
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including new-born screening)	*See Action 39, Priority 3, Goal 7 (newborn screening),* ***International context*** Another central area in the diagnosis of rare diseases is screening examinations. According to an EU-wide evaluation of newborn screening programs for rare diseases in the Member States, Austria operates one of the most extensive programmes in the world in this area (European Commission 2006). ***National context*** While in the empirical survey on rare diseases in Austria, screening procedures for rare diseases beyond the newborn age were largely rejected by the funding bodies, all survey groups confirmed the need for newborn screening or early diagnostic procedures in the newborn period (Voigtländer et al. 2012). Despite the very high standards of Austrian newborn screening, there are still individual challenges in this area: ▪ lack of an independent body for regular, systematic monitoring and evaluation across all medical disciplines of scientific developments in the field of newborn screening or new therapeutic options for rare diseases that are potentially being screened for ▪ lack of transparent inclusion and exclusion criteria for rare diseases in newborn screening.
Personalised medicine, genomics, genetic counselling	*See Priority 3.* ***International context*** Compared to the clinical expertise centres mentioned in Priority 2, there are no guidelines or criteria for diagnostic laboratories for rare diseases at European level. Although the accreditation standard ISO 15189 is a gold standard for the quality and competence of medical laboratories, the special requirements for rare disease diagnostics are not taken into account. For genetic laboratories, the European project Eurogentest attempts to harmonise genetic testing and genetic counselling at the European level.
Models of care/care pathways	**Appendix 2: The Austrian model for specialised centres for rare diseases** The Austrian step model for specialised centres for rare diseases is based on the basic European concepts for so-called 'centres of expertise'. This stipulates that an expertise centre has the competencies surrounding a defined rare disease or group of rare diseases and is intended to act as a central contact point for patients, other hospitals and resident doctors. In addition, there should be research work in the national and international context. The following characteristics and framework conditions for specialised centres for rare diseases were defined in collaboration with the Expert group for Rare Diseases and the Strategic Platform for Rare Diseases. ▪ Expertise cluster (Type A centre)

	▪ Expertise centre (Type B centre) ▪ Associated centre (Type C centre). ***Type B centre*** The Type B corresponds to the original idea of a 'Centre of Expertise' (in accordance with aforementioned European text documents, and is at the heart of the Austrian tiered model. Type B is a specialised individual centre (for example in the form of a hospital department) for a given group of rare diseases. The area of activity and the specific activity profile are therefore defined by the disease group in question. Type B bundles – in accordance with the definition of a 'centre of expertise' – the competencies around a defined group of rare diseases and acts as a central contact point for patients and various healthcare providers as well as other experts from home and abroad. The Type B centre is the basic building block of the European concept for 'centres of expertise' and their subsequent networking to form ERNs. Consequently, Type B centres are also highly relevant for cross-border healthcare. ***Type A centre*** This expertise centre represents an extension of the single centre idea, as used in the classic B centre. It is defined as a synergistic association of at least three B centres at a topographical location, to which one or more centres can also be connected. The focus of Type A is cross-disease, the integrative association of several centres for defined groups of rare diseases. The activity profile combines two functional levels: serving a defined group of rare diseases at the level of a type B centre; and the supply of additional rare diseases by integrating the individual expertise of specialists involved centres in the parent structure of Type A centre. The formation of an A centre requires that several B centres have already been established at a topographical location. The service profile of an A centre also includes the areas of clinical care, research and training. ***Type C centre*** The associated C centre forms the second supplementary level for the classic expertise centre (type B) in the Austrian tiered model of specialised centres and takes up the idea that Austria has a number of individual experts who, as part of their medical practice, care for patients with selected rare diseases and who dedicate their medical-scientific focus to these diseases or the corresponding group of rare diseases. The Type C centre, like the Type B, is a specialised individual centre for a given group of rare diseases. The Type C centre bundles the competencies around a defined group of rare diseases and acts as a central (if no corresponding B centre exists) or additional (if one does) contact point for patients, other hospitals and resident doctors. A Type C centre can in principle arise from a focus at a university clinic, another hospital or a focus hospital. The service profile of a Type C centre primarily covers the areas of clinical care and research. *Note: for more detail on these centre types, see Appendix 2 of the NAP.se.*
Workforce	*See Priority 6, Actions 55-59.*
European Reference Networks	*See Priority 2, Actions 13-22 (specifically mentioned in Actions 15, 19, 20 and 22).* *See Priority 5 – promoting research – Actions 53.* **Priority 6: Improving knowledge about and awareness of rare diseases** ***International context***

	The Cross-Border Healthcare Directive provides in Article 12 "European Reference Networks", point 2 f) as a possible objective "… to facilitate the virtual or physical dissemination of expertise and to develop information, knowledge and best practices within and outside the reference networks, to share and disseminate and to promote developments in the diagnosis and treatment of rare diseases;" and underlines in Article 13 point a) for rare diseases the need to "sensitise health professionals to the tools available to them at the level of "The Union is available to support the specific diagnosis of rare diseases, in particular the Orphanet database and the European reference networks" (European Commission 2011).
EU alignment and participation	*See Priority 2, Actions 15, 19, 20, 22, 27; Priority 4, Action 41; Priority 5, Actions 50-54; Priority 7, Actions 66-68.* Under the section 'illustration of RDs… action 1: In the Recommendation of the Council of the European Union of June 8, 2009 for a measure in the area of RD, Section II. (Appropriate definition, coding and inventory of rare diseases) states that Member States should ensure that "RD is coded in an appropriate manner can be found in and in all health information systems, and appropriate recognition of the disease in national healthcare and health insurance systems based on the ICD (International Statistical Classification of Diseases and related health problems)" (Council of the European Union 2009). This recommendation particularly considers the use of the ICD-11 coding system, which is being developed under the organizational supervision of the WHO, since the ICD-10 depicts rare diseases in an extremely rudimentary manner. To date, there has been no agreement on the mode of integration of rare diseases in the ICD-11 development process; In general, completion is currently not foreseeable. Individual member states are now taking other approaches to developing suitable coding systems. The German Ministry of Health commissioned DIMDI (German Institute for Medical Documentation and Information) 2 to develop its own coding for rare diseases (project duration: 3 years). This builds on the existing ICD coding and allows a link to the approximately 7,000 "Orpha Codes" from the Orphanet database for rare diseases, so no parallel coding is necessary. **Under the section 'improving medical and clinical care… action 2:** The establishment of specialised centres for rare diseases in the individual European Member States and their subsequent networking at the European level has been one of the central concerns of the European Union for more than a decade. The EU's efforts are guided, among other things, by the fundamental idea that rare disease is one of the Form areas in which intensified cooperation at the European level leads to significant added value for all residents of Europe. For this reason, over the last ten years, various European committees and institutions have dealt with various aspects of the topic of rare diseases and published their work results in a series of text documents. This preparatory work ultimately formed an essential basis for the elaboration of the EU's three key policy documents on the subject of rare diseases: the Commission Communication of 2008, the Council Recommendation of 2009 and the Directive of the European Parliament and of the Council of 2011. They also flowed also in the development of the recommendation of the European Union Committee of Experts on Rare Diseases (EUCERD) on possible quality criteria for specialised centres for rare diseases (EUCERD 2011). *(The essential content of these 4 documents is described on page 22/23 for more information, if required).* The 2009 European Council Recommendation does not explicitly mention the establishment of a national coordinating body for RDs, although experiences from other countries such as B. Italy and Germany show that it makes sense and is necessary to have a central national contact point or information hub for rare diseases. The free-to-use online database for rare diseases Orphanet (Orphanet 2011), which was launched in France in 1996, represents the world's most comprehensive information system for rare diseases. On the one hand, Orphanet contains a directory of services including clinics and

	outpatient clinics, laboratories, self-help groups, registers, biobanks, as well as research projects and clinical studies in the partner countries, on the other hand an encyclopaedia with overview articles and/or short summaries. **Action 3 – no alignment (other than that noted under 'personalised medicine' below).** **Under the section 'improving therapy…' Action 4:** The Council Recommendation of June 8, 2009 for action in the field of rare diseases stipulates in Section V (pooling expertise on rare diseases at European level) that member states should pool existing expertise and facilitate the pooling of this knowledge with European partners a number of objectives, including through (Objective 17 e): "…the sharing at EU level of assessment reports on the therapeutic or clinical added value of medicines for rare diseases, so that these medicines can be made available to patients suffering from rare diseases to be available more quickly to those suffering from illnesses" (Council of the European Union 2009). International cooperation is important, among other things, in order to obtain meaningful case numbers for the respective disease, which are essential for a benefit assessment. **Under the section 'promoting research…' Action 5:** A successful example of European research collaboration in the field of rare diseases is the E-Rare project (ERA-Net for Research Programs on Rare Diseases) (ERA-Net 2013), which aims to network research in the field of rare diseases within Europe through regular planning and Publication of transnational tenders followed. Austria is represented by the Fund for the Promotion of Scientific Research (FWF), which has participated in four calls for proposals since 2006 and approved a total of nine Austrian sub-projects with a total funding amount of €1.8 million. **Under section 'improving knowledge…' Action 6:** The Council Recommendation of 8 June 2009 for action in the field of rare diseases (Council of the European Union 2009) stipulates in Section V. (Bringing together expertise on rare diseases at European level) that member states have knowledge of existing expertise in their country on rare diseases and support the pooling of this knowledge with European partners towards a number of objectives, including through: the exchange of best practices regarding diagnostic tools and medical Care as well as education and social care in the field of rare diseases. Appropriate training and education for all healthcare providers "To raise awareness of these diseases and to provide information about the resources available for care in these cases..." the expansion of medical training in areas relevant to diagnosis care for rare diseases are important...". **Under section 'improving epi…' Action 7:** Several other committees set up by the European Commission have dealt with the topic and have identified the particular importance of epidemiological measures for rare diseases in their recommendations (EUCERD 2011; EUROPLAN 2013), although no final decision has been made regarding common minimum data sets became. The EU also funded several research projects that focused on the feasibility (EPIRARE 2013) and the interoperability (PARENT 2013) of epidemiological platforms. In this context, it is particularly worth mentioning that the European Commission is commissioning the EU-funded Joint Research Centre Ispra to set up a European platform to record the various registers for rare diseases in the Member States. **Under Action 8:** The Council Recommendation of 8 June 2009 for action in the field of rare diseases provides under Section VI. (Co-determination of patient associations) stipulates, among other things, that "…patients and patient representatives must be consulted on strategies for rare diseases" (Council of the European Union 2009). **Under Action 9:** The Council Recommendation of 8 June 2009 for action in the field of rare diseases (Council of the European Union 2009) provides under Section VI. (Co-determination of patient associations) sets the following goals: "...consult patients and patient

	advocates on rare disease strategies and facilitate patient access to the latest findings on rare diseases." ...promote the activities of patient associations in areas such as awareness-raising, capacity building, training, exchange of information and best practices, networking and support for very isolated patients..." , The UN Convention for Persons with Disabilities also pursues a comparable goal of involving those directly affected, which provides for the consequences in Article 4 "General Obligations", Paragraph (4): "…in the development and implementation of legal provisions and political concepts In the implementation of this Convention and in other decision-making processes on matters affecting persons with disabilities, States Parties shall consult closely and actively involve persons with disabilities, including children with disabilities, through their representative organizations." In Germany, promoting self-help is a legal responsibility of health insurance companies and their associations. Self-help groups can receive funding in accordance with Section 20 of the Social Code (SGB V) if certain funding principles are met. The funding principles of the umbrella association of statutory health insurance (GKV) describe the framework for the implementation of funding, define the content and procedures of funding and contribute to a largely uniform application of the law in funding practice. The application increases the transparency of the funding process (GKVSpitzenverband 2013).
Health information (including rare disease registries)	*See Priority 7, Actions 64-68.*
Orphan medicines	*See Priority 4, Actions 41-49.* The European Commission supports a wide range of activities to improve access Orphan Drugs at European level, with the following two key and current initiatives: ▪ Cooperation between the European Medicines Agency EMA (European Regulatory Authority 2013) and the European Network for Health Technology Assessment (EUnetHTA 2013), an essential part of which is the further development of the dialogue ("Early Dialogue") on the effectiveness of orphan drugs before their approval (European Medicines Agency 2013). Austria was involved in this cooperation from the beginning. ▪ The "Mechanism of Coordinated Access to Orphan Medicinal Products (MoCA OMP)" initiative in the context of the EU platform "Access to Medicines in Europe" (European Commission 2013) also aims to establish an "early dialogue" between industry and payers start to discuss possible "unmet medical needs" before a new product is developed. Clinical studies should provide information relevant not only for approval but also for future payers of the medication (for example, for benefit assessments and price negotiations). **Priority 4: Improving therapy and access to therapies for those affected by rare diseases** In the report "Rare diseases in Austria" (Voigtländer et al. 2012), access to medicines was rated as very good by the majority of patients with SE or other stakeholders surveyed, but some problem areas in the area of medication were also identified therapy identified. The key messages of the report are: ▪ Financial expenses for orphan drugs in the private sector: In 2012, social insurance spent around €2.7 billion on all reimbursed drugs. Of this, approximately €106 million was spent on orphan drugs. At the beginning of 2012, 51 of the 62 orphan drugs approved in the EU were available in Austria. While the average cost per medicinal product prescription in the private sector was €21.33, the average cost of a prescription for an orphan drug in the private sector was over €2,700 in 2012. These figures show that orphan drugs almost always have very high prices. The arguments for this include both the high development costs coupled with small case numbers on the one hand and the monopoly position of the providers on the other. ▪ Inadequate representation or coverage of treatment costs for rare diseases including costs for orphan drugs in the inpatient billing system. ▪ The amount of expenditure for drug therapies (including orphan drugs) in the inpatient area is not known.

	▪ Financial and structural challenges due to cross-state or cross-border healthcare. ▪ Nationwide uniform reimbursement of costs for medical devices: Although the prescription of medical devices is subject to the social health insurance guidelines on the economical method of prescribing medicines and medical devices, there is no uniform catalogue of services for the reimbursement of medical devices. ▪ Unclear financing structure at the interface between hospital outpatient and inpatient care area. ▪ Unclear financing structure at the interface between outpatient/inpatient and community-based areas. ▪ Often high private financial expenses of patients with rare diseases. ▪ Hurdles in approving therapies.
Rare disease research	In 2012, the NKSE published an extensive empirical survey on behalf of the BMG, the aim of which was to record the problems of those directly affected as well as the people and institutions professionally involved in the issue and to identify possible errors and identify deficits in the supply system. In addition, the study contains opinion trends and priorities for possible solution scenarios that were included in the development of the NAP. [*Title: 'Rare diseases in Austria' (Voigtländer et al. 2012)*]
Alignment beyond the healthcare sector	*See Priority 9.*
Any additional information (for example, background to the strategy or strategy development)	The National Action Plan for Rare Diseases (short title: NAP.se) was developed on behalf of the Federal Ministry of Health (BMG) by the National Coordination Centre for Rare Diseases (NKSE) in collaboration with the two advisory bodies – Expert Group for Rare Diseases and Strategic Platform for Rare Diseases. Four starting fields to create the Plan: 1. European requirements 2. NKSE publication 'Rare Diseases in Austria' (2012) 3. More structured exchange with national experts 4. More national connecting points.

Key: AGES: Austrian Agency for Health and Food Safety; ARGE self-help: Working Group for Self-Help Austria; AWS: Austrian Business Services Society; BMG: Austrian Federal Ministry of Health; BMWFW: Federal Ministry of Science, Research and Economy ; EMA: European Medicines Agency; ERNs: European Reference Networks; EUCERD: European Union Committee of Experts on Rare Diseases; EUnetHTA: European Network for Health Technology Assessment; FFG: Austrian Research Promotion Agency; FWF: Fund for the Promotion of Scientific Research; GÖG: Austrian National Public Health Institute; GKV: Austrian umbrella association of statutory health insurance; HVB: Central Association of Austrian Social Insurance Institutions; ICD-10: International Classification of Diseases 10th Revision; ICD-11: International Classification of Diseases 11th Revision; ISO: International Organization for Standardization; MoCA OMP: Mechanism of Coordinated Access to Orphan Medicinal Products; NAP.se: National Action Plan for Rare Diseases; NKSE: National Coordination Centre for Rare Diseases; ÖÄK: Austrian Medical Association; PHARMIG: Association of the Austrian Pharmaceutical Industry; PharMed: Continuing education and networking platform for organisers of medical training events; SV: Social Insurance.
Note: The information in this table was extracted from a version of the original document translated to English using Google Translate.

Table B4. Data extracted for Austria (National Action Plan Executive Summary)

Austria	Strategy information
Author(s) **Title**	Austrian Ministry of Health (*Bundesministerium für Gesundheit*, BMG) and Austrian National Public Health Institute (*Gesundheit Österreich GmbH*, GÖG) Austrian National Action Plan for Rare Diseases (Executive Summary)[49]
Timeline	2014-2018
Overall aim(s)	To improve the lives of all patients with rare diseases – involving their families as well as their professional and social environment – irrespective of age, gender, extent of disability or socio-economic status.
Themes and or priorities	The Plan contains nine core areas, also known as 'fields of action', which take into account European recommendations and national requirements: 1. Mapping of rare diseases in the healthcare and social system 2. Improvement of medical/clinical care for rare disease patients 3. Improvement of diagnostics of rare diseases 4. Improvement of therapy and access to therapies for rare disease patients 5. Promotion of research in the field of rare diseases 6. Improvement of general knowledge with respect to and awareness of rare diseases 7. Improvement of epidemiology in the context of rare diseases 8. Constitution of permanent advisory bodies for rare diseases at the Ministry of Health 9. Acknowledgement of the merits of patient organisations for rare diseases.
Targets (if specified) and measurement method(s) (where available)	See full text for goals.
Implementation action(s), lead(s) and key performance indicator(s)	The Austrian National Action Plan for Rare Diseases combines plan and strategy. Each 'field of action' had defined objectives and corresponding measures based on the assessment of the existing situation. Sample objectives are: ▪ Rare diseases and rare disease patients should be made more visible. The Plan makes provision for the establishment of a comprehensive epidemiological platform for patients with rare diseases, in order to register rare disease cases in Austria. The initiative will be coordinated with existing national and international activities to guarantee the interoperability with current systems. ▪ In order to document medical service costs provided for rare disease patients, the Plan introduces a documentation/coding system for rare diseases as a primary goal. ▪ Regarding the provision of health services the Plan focuses on improved coordination of clinical care by designating specialised centres for rare diseases (centres of expertise), and their subsequent interconnectedness within Austria and within the relevant European Reference Networks (ERN). ▪ The Plan does not propose the establishment of new structures but to concentrate expertise which already exists – meeting quality criteria and certain standards – in supra-regional centres. ▪ It is envisaged that intensified cooperation would facilitate a maximally efficient use of highly specialised resources and expertise, leading to improved diagnostics, therapy and clinical care of rare diseases. ▪ The Plan envisages that continuous access to Orphan Drugs will be optimised.

	▪ rare disease patients should receive a faster clinically reliable diagnosis. The Plan suggests that as well as improved clinical care, nationwide diagnostic standards should be implemented as well as the concentration of diagnostic expertise. ▪ The Plan defines specific measures, amongst others in the field of primary care: to overcome the knowledge deficits with respect to rare diseases, to promote rare disease awareness and to improve access to reliable and objective information. ▪ Primary care physicians are largely the first point of content in the healthcare system. Patient safety and health competence should be strengthened by quality assured, objective and target-group specific information which would indirectly facilitate access to the 'best point of service'. ▪ Considering that patient organisations greatly contribute to the care of patients with rare diseases, the Plan aims to make the services and achievements of these organisations more visible and to acknowledge the expertise and experience of patients and relatives, as well as utilising this expertise in the context of national activities and developments. Patient organisation representatives played a major role in the Plan's development. The implementation process of the National Action Plan, as well as its success will be monitored by specific indicators for each field of action. Indicators are defined in accordance with European developments and actions. Variety and complexity of the measures stated in the national plan require the definition of indicators in the course of the implementation process of each respective measure. This allows for the consideration of current developments and potentially necessary adaptations.
Governance and organisational structures	The National Coordination Centre for Rare Diseases developed the plan, along with two advisory committees: the strategic platform for rare diseases and the expert group on rare diseases (on behalf of the Austrian Ministry for Health).
Funding model	*Not mentioned.*
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	*Not mentioned.*
Personalised medicine, genomics, genetic counselling	*Not mentioned.*
Models of care/care pathways	*Not mentioned.*
Workforce	*Not mentioned.*
European Reference Networks	*Please see third bullet point under 'Targets' regarding reference to ERNs.*
EU alignment and participation	Excerpt from the section: 'themes and or priorities' above – The Plan contains nine core areas, also known as 'fields of action', which take into account European recommendations and national requirements

Health information (including rare disease registries)	*Not mentioned.*
Orphan medicines	See 'targets' section above: The Plan envisages that continuous access to Orphan Drugs will be optimised.
Rare disease research	*Not mentioned.*
Alignment beyond the healthcare sector	*Not mentioned.*
Any additional information (for example, background to the strategy or strategy development)	The plan was developed by the National Coordination Centre for Rare Diseases (Nationale Koordinationsstelle für Seltene Erkrankungen, NKSE) on behalf of the Austrian Ministry of Health, in cooperation with two advisory committees, the expert group on rare diseases (from 2014 advisory committee for rare diseases), and the strategic platform for rare diseases. Starting points for the national plan were European requirements (e. g. recommendations, guidelines), the national empirical survey 'Seltene Erkrankungen in Österreich' ('Rare diseases in Austria', Voigtländer et al 2012), the structured exchange with national experts, and current national developments such as the definition of health targets (Rahmen-Gesundheitsziele), the healthcare reform or the Child and Youth Health Strategy (Kinder- und Jugendgesundheitsstrategie). Also see last bullet point under 'targets' above i.e. Patient organisation representatives played a major role in the Plan's development.

Key: BMG: Austrian Federal Ministry of Health; ERNs: European Reference Networks; GÖG: Austrian National Public Health Institute; NKSE: National Coordination Centre for Rare Diseases.

Note: The information in this table was extracted from a version of the original document translated to English using Google Translate.

Table B5. Data extracted for Austria (Evaluation of National Action Plan)

Austria	Strategy information
Author(s) **Title**	Gesundheit Österreich GmbH (GÖG) (On behalf of the Federal Ministry for Social Affairs, Health, Care and Consumer Protection) Evaluation of the NAP for rare diseases[48]
Timeline	Evaluation conducted between December 2019 and March 2020 (NAP ran from 2014-2018)
Overall aim(s)	The aim of the evaluation of the NAP.se is to examine to what extent it was and is suitable, through increased networking of involved stakeholders in the area diseases to improve the processes and information for those affected by them. The primary users of the evaluation are its clients, as well as actors in connection with the NAP.se, and representatives of people with rare diseases.
Themes and or priorities	The evaluation should address the following questions: ▪ According to the assessment of the stakeholders involved, do the actions in NAP lead to an improved living situation for people with rare diseases in Austria? ▪ What is the degree of implementation of the actions? What are the reasons that some actions were implemented and others were not? ▪ What are the assessments regarding the creation process? Were the various relevant stakeholders sufficiently involved in the preparation and implementation of the NAP.se? ▪ Were the main challenges faced by people with rare diseases managed through appropriate actions? ▪ How should the further implementation of the actions be promoted? ▪ How was the financing of the actions secured? ▪ What learning experiences can be derived for the further implementation of the actions?
Targets (if specified) and measurement method(s) (where available)	Interviews: 14 guided expert interviews (some individually and some in groups) were conducted with a total of 19 representatives of the expert group and the strategic platform Survey: Online questionnaire sent to a total of 22 representatives from the Expert Group and Strategic Platform. Fifteen responses received.
Implementation action(s), lead(s) and key performance indicator(s)	**According to the assessment of the stakeholders involved, do the actions in NAP.se lead to an improved living situation for people with rare diseases in Austria?** The results of the evaluation show three trends in particular: 1. Initial progress and positive effects: The structures (Advisory Board for Rare Diseases and Strategic Platform) were created and implemented to a high degree. The designations of the expertise centres have been sufficiently implemented and have gained momentum. The designation process contributed to raising awareness in the community. The established expert groups also made it possible to increase the flow of information. Diagnostics have also improved thanks to the expertise centres, as there are clearer contact points for those affected. Since communication between the centres has also increased, this may lead to more targeted allocation behaviour. At the same time, quality assurance could be improved… according to individual interviewees, the effect of creating the areas of competence is on the right track. Transparency is mentioned several times as a major benefit of NAP.se. 2. Difficult to assess the impact of NAP.se: However, according to most interview partners, it is difficult to assess whether the effects mentioned have a direct connection with the NAP.se. A very general assessment is that the NAP.se leads to an improvement. However, it is not clear whether individual measures are effective or whether effects arise in general because the NAP.se exists as an action plan. According to individual experts, the good care for people suffering from rare diseases is, for example, due to the fact that technological innovations are quickly adopted in Austria. This rapid mapping generally has a positive impact on patient care.

	3. Little to no effect: Some experts and stakeholder representatives – especially from the medical field, self-help, social security and the pharmaceutical industry – have so far seen little to no effect on improving the living situation of people with rare diseases through NAP.se. Of all nine fields of action, not a single measure has been implemented 100 percent – with the exception of the establishment of a permanent advisory committee in the health department. The NAP.se currently has very little immediate effect. **What is the degree of implementation of the actions? What are the reasons that some actions were implemented and others were not?** Overall, the respondents considered the level of implementation of the actions to be rather low. For the majority of measures (69 of 82) the estimated level of implementation was less than 50%. Field of action 7 (epidemiology of rare diseases) was estimated to be the lowest; the degree of implementation for every action in that field was estimated to be less than 15%. The explanation given in the interviews was that there is generally hardly any investment in the field of epidemiology in Austria; this applies to all diseases, not just rare diseases. An exception to the trend of a generally low level of implementation can be seen in field of action 2, goal 2 (designation of specialised centres for defined groups of rare diseases). The values in field of action 8 (committees) are also higher than in the other fields of action. The most common reason why measures have not (yet) been implemented or not fully implemented is the lack of clarity regarding the financing of implementation was mentioned, partly also a lack of monitoring of implementation, but also the prioritisation in favour of the designations. Some also noted that further implementation would require increased inter-sectoral cooperation and coordination between the federal/state governments and social security. **What are the assessments regarding the creation process? Were the various relevant stakeholders sufficiently involved in the preparation and implementation of the NAP.se?** Almost all experts and stakeholders stated that in principle all relevant stakeholders were involved in the creation process of NAP.se. However, some interviewees noted a certain "medicine bias" and it seemed sensible to them to include other disciplines for further implementation in the spirit of Health in all Policies, such as representatives of the social sciences, education system, and the disciplines of nutritional advice, occupational and physiotherapy. There are different perceptions about the process itself; some interviewees stated that the process was not very structured, and the role of the NKSE is also viewed critically in this context. Some experts particularly missed transparent, structured information within and between the two committees, which they would have seen as the task of the NKSE. One expert noted that although there was an opportunity to submit statements, these were not taken into account – without justification or discussion. In his opinion, the process as a whole was not transparent enough. Another interviewee was satisfied with the creation process. **Were the main challenges faced by people with rare diseases managed through appropriate actions?** Most experts and stakeholders considered the measures depicted in NAP.se to be generally well suited. However, individual interviewees also saw some challenges. Accordingly, the concentration of implementation has so far focused too much on the topic of designations. Although the designation process for centres of expertise has initially set a useful focus, other measures would have to be considered for many other existing rare diseases. A special objective would also be a measure to reduce the time required for diagnoses. One of the most common topics for those affected is finding a diagnosis. The problem is also that therapies can only begin after a diagnosis. The measures also do not sufficiently reflect the connection between those affected and the social and educational system (in the sense of Health in All Policies), but this would reflect the reality of life of those affected- very important. There is also a lack of involvement of several health and social professional groups (for example, nurses, physiotherapists and psychologists). **How should the further implementation of the actions be promoted? How was the financing of the actions secured?**

	All experts and stakeholders stated that the question of financing had been deliberately left out. Some report that in the discussions in the Strategic Platform and the Advisory Board for Rare Diseases it was repeatedly stated that the NAP.se should not incur any additional costs. At the moment there is also a lack of clear objectives and indicators; The objectives of the coordination office are also not clear. There is also a lack of clear commitment from the financiers involved when it comes to implementation. With regard to the implementation of the measures, the majority of the experts and stakeholders surveyed were in favour of setting appropriate priorities with schedules, clear responsibilities and milestones over several years for the measures that have not yet been completed or those that are still outstanding. Appropriate monitoring should also be provided. Some interviewees suggested creating a slimmed-down new version of NAP.se, but one that would be feasible and more concrete. Appropriate financing of the measures should also be taken into account. This could take the form of an implementation plan coordinated with all stakeholders involved. **What learning experiences can be derived for the further implementation of the actions?** ▪ Improved communication and information among committees: Improvements required to communication both within and between the committees; for example, updates on the implementation status of the actions. This was seen as a task for the NKSE. ▪ Transparency: Several representatives of the Advisory Board and the Strategic Platform identified that the creation process of NAP.se was not transparent enough. As a result, communication internally and externally was relatively non-transparent. Information about activities that have already been carried out and those that are still planned, as well as clear priorities and strategic directions, must be clearly communicated. ▪ Role of the NKSE: Some experts and stakeholders said that it was not clear who was responsible for implementing the NAP.se and coordinating the process. Some also said that there was too strong a focus on designations, which pushed the implementation of other actions into the background. International networking should be the responsibility of the centres of expertise, and the focus of the NKSE should be on coordination and implementation of national activities. ▪ Duration and procedure of the designation process: The fact that the designation process is slow and has already taken many years was viewed critically by all interviewees. The duration, intensity, complexity, and resource-consuming nature of the process were noted. It has led to a high level of frustration among those involved. However, some experts and stakeholders pointed out that strict testing makes sense, as quality assurance is necessary. **Recommendations for action** For the further implementation of the NAP.se, the following recommendations for action can be derived based on the evaluation and the answers to the research questions: 1. Essential for greater clarity regarding the further implementation of the NAP.se is a transparent presentation of the tasks of the NAP.se committees: the NKSE, the national office (NB-NAP.se), the Advisory Board for Rare Diseases and the Strategic Platform. 2. In this context, it should also be clarified who is responsible for the project and process management of the further implementation of the NAP.se. As part of project and process management, it should then be determined how the flow of information between the committees should be ensured. 3. In order to promote further implementation of the NAP.se, an implementation plan that is as broad as possible appears to be a recommended next step. The aim of this plan should be to make it clear to all stakeholders and experts involved what is possible/realistic and what is not. The implementation plan should definitely contain the following points: ▪ a prioritisation that is feasible according to the assessment of the relevant stakeholders measures ▪ a clear scheduling of the measures based on prioritisation ▪ clear responsibilities for implementation and financing

	▪ a determination in what form and by whom the further monitoring will be carried out implementation should take place ▪ organising and coordinating the creation of the implementation plan is another task within the scope of project and process management. 4. Subsequently, monitoring of the implementation of measures should be carried out – as in the implementation plan determined – carried out on an ongoing basis.
Governance and organisational structures	The National Action Plan for Rare Diseases 2014-2018 (NAP.se) was developed on behalf of the Federal Ministry of Health (BMG) by the NKSE in collaboration with two advisory bodies, the Expert Group for Rare Diseases and the Strategic Platform for Rare Diseases. The NAP.se sets nine central thematic priorities (= fields of action) that take into account both the European recommendations and national requirements in the area of rare diseases. The NAP.se provides for monitoring and evaluation of its implementation. The Ministry of Social Affairs commissioned GÖG to evaluate the NAP.
Funding model	The most common reason why measures are not (yet) implemented or not fully implemented was the lack of clarity regarding the financing of implementation, partly also a lack of monitoring of implementation, but also the prioritization in favour of designation. All experts and stakeholders stated that the question of financing had been deliberately left out. Some report that in the discussions in the Strategic Platform and the Advisory Board for Rare Diseases it was repeatedly stated that the NAP.se should not incur any additional costs. A majority of the experts and stakeholders surveyed stated that the NAP.se was an action plan that did not take financial considerations and was not predetermined have a schedule. Some call it a declaration of will. At the moment there is also a lack of clear objectives and indicators; The objectives of the coordination office are also not clear. There is also a lack of clear commitment from the financiers involved when it comes to implementation have a schedule. Some call it a declaration of will. At the moment there is also a lack of clear objectives and indicators; The objectives of the coordination office are also not clear. There is also a lack of clear commitment from the financiers involved when it comes to implementation. With regard to the implementation of the measures, the majority of the experts and stakeholders surveyed were in favour of setting appropriate priorities with schedules, clear responsibilities and milestones over several years for the measures that have not yet been completed or those that are still outstanding. Appropriate monitoring should also be provided. Some interviewees suggested creating a slimmed-down new version of NAP.se, but one that would be feasible and more concrete. Appropriate financing of the measures should also be taken into account. This could take the form of an implementation or implementation plan coordinated with all stakeholders involved. **Findings from interviews with experts** In relation to research, in Austria there is no national programme or financial pot for funding for rare diseases. The centres are therefore left to their own devices and will seek cooperation and submission for possible third-party funding. HVB has repeatedly distanced itself from the role of financier, which is difficult, however, as this role is of course in the nature of the matter. The roles were more passive and less active. The funding pot for rare diseases has always been an issue – with approaches such that, for example, every federal state must create a pot so that each federal state also focuses on rare diseases, also with financial consideration. It was regularly discussed that politicians and financiers needed to be brought on board. That's why there were no concrete timelines and concrete measures. Ultimately, it is an action plan that has no financial consideration and no specified timetable. So it is more of a guide or a declaration of intent.

	An unintended effect is that clinics are financed in such a way that they cannot afford the care of those affected by rare diseases, i.e. they do not want the patients because they cannot afford their care. Although the provision was intended, this intention went in the wrong direction. Although some experts on the Advisory Board for Rare Diseases repeatedly raised the lack of funding as problematic in the meetings, the ministry tended to ignore this topic. A budget or financial plan has not been drawn up to date, but from the social security representatives' point of view it would be necessary. With regard to field of action 9, the social security representative commented as follows: The Pro-Rare representatives have regular exchanges with the umbrella organisation and are now also represented in some committees (for example, patient advocates in the Therapeutic Products Evaluation Commission). This is an ongoing process. One problem is that self-help groups are often supported by the pharmaceutical industry. Public financing should therefore be considered. This is fundamentally a political question: if you want to involve patients, financing must also be ensured. In the case of self-help, regulated independent financing would also be a solution so that self-help groups or organisations no longer have to finance themselves exclusively through donations.
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	A scientific committee for Austrian newborn screening was set up. The Advisory Board for Rare Diseases did not originally prioritise Goal 8 of Priority (field of action) 3, the "Development of an Austrian 'Undiagnosed Diseases Programme'", and it would have to be re-evaluated before being processed.
Personalised medicine, genomics, genetic counselling	*Not mentioned.*
Models of care/care pathways	*See 'implementation' above.* Specifically the evaluation refers to improved diagnostics thanks to expertise centres and clearer points of contact, but quality assurance could be improved. With expertise centres diagnostics become more targeted, creating a more structured approach. Avoiding diagnostic errors avoids unnecessary costs. Almost all experts and stakeholders stated that in principle all relevant stakeholders were involved in the creation process of NAP.se. However, some interviewees noted a certain "medicine bias" and it seemed sensible to them to include other disciplines, such as representatives of the social sciences, for further implementation in the spirit of "Health in all Policies", and education system, but also the disciplines of nutritional advice, occupational and physiotherapy, as this is very important for the reality of life of those affected. The following excerpt is from interviewees: Holistic care: Holistic care (physiotherapy, remedies and aids, nutritional advice) for people with rare diseases would be essential; the expertise centres could be pioneers here. The social and educational systems are currently not integrated into the NAP.se at all (in the sense of "Health in all Policies"). In this context, a survey of self-help groups is a useful suggestion (keyword: more creative approach, for example, with regard to the holistic care of those affected and their families or relatives).

Workforce	*(Taken from an individual interview)* Financing the implementation of the measures: In this context, it is also about human and time resources that have to be linked to the measures. So need also the provision of personnel support for a certain period of time (for example, to generate appropriate knowledge). Careful consideration must therefore be given to which resources could actually be used to implement which measures and within what time frame. There should be no excessive demands on those involved. Of course, implementation also requires a certain amount of financial resources and a certain degree of competition arises between the topics. At the beginning of measures, one must also ensure that there is a long-term, continuous resource and the necessary partners for implementation. Otherwise the implementation of measures is not sustainable.
European Reference Networks	At the beginning of the implementation of NAP.se, the Advisory Board for Rare Diseases defined priority measures including key actors in charge in order to strengthen the commitment to implementing the action plan and encourage all actors to proactively plan and act. Particular priority was given to action area 2 (medical-clinical care) and in particular to the designation of centres of expertise for rare diseases, as current developments (the establishment of the European Reference Networks [ERN] at EU level) were taken into account when implementing the measures are, which is still the case. The designation process is not yet complete. So far, nine expertise centres have been designated. The first two designated centres are also represented as full members in the ERNs. At the EU call in November 2019, seven Austrian expertise centres applied for full membership in the ERN (the completion of the EU procedure has been postponed to 2021 due to the COVID-19 pandemic). In order to achieve a connection to all 24 ERNs, the Ministry of Health reported a further 41 institutions to the European Commission as associated national centres. Associated centres would have access to the ERN's Clinical Patient Management System, meaning they could submit case discussions. This means that patients can be guaranteed access to all 24 ERNs.
EU alignment and participation	**Findings from interviews:** From the point of view of the representative of the federal government, all relevant stakeholders were involved in the preparation process. In order to achieve a commitment by all parties involved to the NAP.se as a strategy and plan for rare diseases, a pragmatic solution was agreed and financing and financing was excluded. This approach was justified, among other things can that for example, It was always planned and communicated in the designation of the expertise centres that no new structures should be created, but rather existing expertise should be made visible. The Ministry of Health tried to adapt the development of the NAP.se to EU-wide strategies on the subject of rare diseases for example, to coordinate the structure of the European Reference Networks (ERN) in terms of definition and content. By adopting the criteria that the EU has defined for the admission of full members to the ERN as criteria for the designation process of expertise centres in Austria resulted in the "strict" designation process, which aims to make outstanding expertise visible. However, these strict criteria are no longer applied to this extent in the EU. It was not intended that, in contrast to other EU member states, which are represented by a large number of full members in the ERN, Austria has so far only taken part in the second EU call with two full members and seven applications. On the one hand, this could be seen as a result of the slow implementation of the NAP.se and in particular the designation process, but on the other hand, the developments at EU level could not have been predicted. The criteria for the Austrian designation process are aligned with the EU's original criteria for the admission of full members to the ERN. In Austria, these criteria and a corresponding process have been agreed upon and we are sticking to these criteria in the ongoing process. Some member states of the European Union do not have a designation process and have abandoned the original criteria – according to which a centre only receives the support of the health authority to apply as a full member of an ERN if it has outstanding expertise. This

	resulted in an imbalance in the number of centres per Member State and for patients – does not ensure that all centres in an ERN have outstanding expertise. The orientation for the objectives within the NAP.se was very closely aligned with the European guidelines in terms of structure and measures. The designation of expertise centres (field action 2) should be applied to the same across the EU. Unfortunately, the situation is very heterogeneous, because some countries only bring in the "lighthouse centres" – as originally planned – while other countries would allow all interested institutions to be centres of expertise in the European network. The EU should urgently work on standardisation so that the idea of expertise centres does not lead to absurdity. There is criticism in Austria of the way the process has been set up in Austria. However, this process is designed as the EU originally intended. The expertise centres would have to be staffed in accordance with the criteria and have sufficiently high number of cases.
Health information (including rare disease registries)	**Findings from interviews:** With regard to field of action 1 (representation of rare diseases in the health and social system), the social security representatives report that there is currently no standardised diagnosis coding in the private practice sector (intramural yes, extramural no) measures in the area. They would therefore consider it to be pointless until standardised diagnosis is implemented established area. Furthermore, the ICD-10 is probably not sufficiently granular to adequately depict rare diseases. The ICD-11, which is intended to allow more sophisticated encryption, will only come into force in a few years. It would be important if a patient was diagnosed with a rare disease by a centre that their treating physician would take over the diagnosis from the centre. From the perspective of the federal representative, the focus in field of action 1 should not be too much on this. It is important to represent the rare diseases in the ICD-10 diagnostic classification, since this classification key is primarily specified by the WHO and in the next five should be replaced by the ICD-11 in years. He doubts that the ICD-11 classification will be so differentiated that it covers all rare diseases and that it will ever be able to do this. In his view, work must be done to equip the expertise centres with suitable documentation systems that enable an international exchange of information with other centres and with health service providers within Austria abroad. It makes little sense to use complex classification systems for rare diseases among general practitioners or at lower levels of healthcare facilities establish. This would only entail a lot of administrative effort and the quality of the documentation certainly wouldn't be very high. It is primarily the task of the specialised expertise centres to make the diagnoses correctly and to document them using suitable classification systems. Communication between health facilities works via electronic health records, where the medical data should be recorded correctly, as long as this data is important for further treatment or for other treatments. In electronic health records, findings, secondary illnesses and therapies should be accurately depicted so that patients, if they were treated in other health facilities, could be treated correctly by the doctors working there. The federal representative therefore does not expect that his own detailed documentation of rare diseases will be created, but rather that the cases will be well represented in electronic health records so that patients have a correctly maintained, complete health record that can also be used as a basis for treatment abroad.
Orphan medicines	*The only reference to "orphan drugs" was in relation to their cost possibly increasing (page 31). However there is a reference to the Orphan Drugs Network in the implementation of measures section 4.1.7.2 (see below).* From the perspective of the federal state representation, a representation of rare disease in the health and social system (field of action 1) has not been implemented. A uniform documentation is not possible at the moment, and Austria is still years away from that. The visualisation is achieved in part by the Orphan Drugs network, not by the NAP.se. The medical clinical care for people suffering from rare

	diseases (field of action 2). Part of general curative care. In general, the situation regarding rehabilitation for children has improved, but it is difficult to assess whether this is due to the NAP.se. The designations are the only visible measure. The designations of the expertise centres have been sufficiently implemented and have gained momentum. There is hardly any investment in Austria in the area of epidemiology (action area 7), but this applies to all diseases and not just rare diseases. The structures created (the advisory board for rare diseases and the strategic platform, field of action 8) have been implemented to a high degree. In recent years there have been improvements in the area of self-help (action area 9), it is also generally valuable and worth supporting, but there is no discernible connection with the NAP.se.
Rare disease research	A research representative who was involved in the creation process of NAP.se from the beginning took part in this interview as part of the evaluation of the plan. The Ministry of Science was also part of the Advisory Board for Rare Diseases from the beginning and there was a nomination process. The aim was to make research contributions to the fields of action. According to the research representative, the topic of rare diseases has become more visible (field of action 1), for example in the population. B. through campaigns in which there are also advertising campaigns for certain rare diseases. This is also accompanied by a certain level of awareness. In connection with the designation process (field of action 2), the medical universities would express great interest in setting up centres of expertise. There has often been criticism that the designation process is very lengthy and, in comparison with other countries, raises the question of whether this process is actually effective in Austria. The criticism is that potential Austrian centres of expertise would lose touch with the European network and would feel excluded, particularly when it comes to research. With regard to improved care, it should also be asked whether such a restrictive process is in the interests of the patients. In terms of measures and goals, the promotion of research (field action 5 of NAP), is more like this aimed at improving the information situation outside the research community. The information situation in the relevant community itself is good, as researchers are well informed about the various calls for proposals by the FWF and FFG (regular newsletters, web pages, etc.). It was more about informing other arears about research, and that also happened through the Advisory Board for Rare Diseases. The mission of the evaluation of this plan is to improve therapies and access to therapies (field of action 4) clear and prescribed. This gives a clear mandate. Access to the therapies is possibly improved in that those affected would have clearer and multiple contact points through the expertise centres. You could also turn to them for appropriate therapies. However, this development was not brought about by the national plan. Access to therapies is generally very good in Austria, in the future it will be more about making even more therapies possible through research. The more resources there are for research (field of action 5), the more research is carried out. This tendency can be observed in general, especially in the pharmaceutical industry. However, the new preparations that are often created through research are often very expensive. This development is but also not triggered by the NAP.se.
Alignment beyond the healthcare sector	Some also noted that further implementation would require increased inter-sectoral cooperation and coordination between the federal/state governments and social security. The measures in the plan do not sufficiently reflect the connection between those affected and the social and educational system (in the sense of Health in All Policies), but this would reflect the reality of life of those affected very important. There is also a lack of involvement of several health and social professional groups (for example, nurses, physiotherapists, psychologists).

	In the expertise centres themselves, there is still room for improvement in terms of communication and the integration of other disciplines. Holistic care (physiotherapy, remedies and aids, nutritional advice) would be essential; the expertise centres could be pioneers here, and the health and social system would have to implement measures in this regard.
Any additional information (for example, background to the strategy or strategy development)	*Further details of findings from interviews with individuals of varying disciplines (page numbers for data extraction included):* ▪ Implementation requires resources and a team (Page 7) ▪ Measures to be sorted and grouped into ones that individuals can implement, with appropriate timeframe (Page 8) ▪ There should be a measure to reduce diagnosis time (Page 8) ▪ Improving awareness of RDs needs more implementation (Page 10) ▪ Coding is important for improving epi knowledge (Page 10) ▪ Communication and transparency re implementation (Page 10) ▪ Recognition for self-help groups (Page 11) ▪ There are something like lighthouses with special illnesses, but no contact point for complex, difficult questions for all people. The goal would be to set up contact points for all people who have any unclear symptoms or questions. There is a lack of an appropriate supply structure (Page 12) ▪ A need for improvement would be to ask the question of whether such a long, restrictive designation process is actually necessary. It is not a matter of every centre that claims to be a centre of expertise being designated, but a pragmatic middle ground would be worth considering. It might also make sense to look at other countries and see how the process was solved there in a pragmatic yet quality-assured manner. Germany would be a country you could look at. The Scandinavian countries also have pragmatic solutions (Page 17) ▪ Clear process management is required (Page 19) ▪ The two social security representatives emphasise that there is a lack of a concrete implementation plan. What use would the measures be if the structures for them did not exist or were not created? "Where should the journey go?" Once this question has been clarified, the next step should be to clarify the processes and create the structures. At the moment, measures are being "popped out of the ground", but the financing and the strategy for concrete implementation are missing. One suggestion is therefore to initially build on existing structures. In their opinion, the prioritisation of the fields of action and goals represents an essential criterion for a concrete implementation plan (goals, budget, structures, responsibilities), which currently does not exist. (Page 20) ▪ The communication between the advisory board for rare diseases and the platform for rare diseases is also perceived by the social security representatives as not very structured. The most important messages would not be conveyed. What would be relevant would be: What happens, how, where and why? (Page 21) ▪ When it comes to expertise centres, the question arises as to whether they are a sustainable structure or whether the expertise depends on an individual doctor. Sustainable structures with interdisciplinary collaboration between a team of doctors would be essential in this context. (Page 24) ▪ In the area of diagnostics (field of action 3), more training on rare diseases would be needed – also in the private sector – necessary, especially with regard to how referrals in the health system should be handled ("Where should unclear cases be sent?"). It is important that the first points of contact are trained and networked. Standardised diagnostic instruments should also be used in this context. Also, international (digital) networking is very important in this context due to the low number of cases. (Page 24) ▪ The designation for an expertise centre will tend to attract those institutions that hope to gain budget funds from it (for example, new private universities). Already established medical facilities, which are basically a centre of expertise anyway, would hardly make any effort to receive an additional label as a centre of expertise. On the one hand, they are already a centre of expertise and on the other hand, the official label could also come with demands for money. It could also be unintended that the number of cases of rare diseases would

	be increased inappropriately. Centres may be inclined to diagnose more patients with a rare disease in order to reach the necessary number of cases. The definition of a rare disease stipulates up to five affected people out of 10,000 people. For example, in the case of amyotrophic lateral sclerosis (ALS), 5.2 people out of 10,000 are already affected, but ALS is still listed as a rare disease. A corridor would have to be created for better regulation. (Page 38)

Key: ALS: Amyotrophic Lateral Sclerosis; BMG: Austrian Federal Ministry of Health; ERNs: European Reference Networks; EU: European Union; GÖG: Austrian National Public Health Institute; HVB: Central Association of Austrian Social Insurance Institutions; ICD-10: International Classification of Diseases 10th Revision; ICD-11: International Classification of Diseases 11th Revision; NAP.se: National Action Plan for Rare Diseases; NB-NAP.se: National Office for the Implementation of NAP.se; NKSE: National Coordination Centre for Rare Diseases.
Note: The information in this table was extracted from a version of the original document translated to English using Google Translate.

Table B6. Data extracted for Denmark (2014 strategy)

Denmark	Strategy information
Author(s) **Title**	The Danish Health Authority National strategy for rare diseases[24] NOTE – There are two further review documents for this strategy in 2018 and 2022. These narrowed the recommendations down to actionable recommendations that could be implemented and therefore our focus is on these updated documents.
Timeline	Published in 2014.
Overall aim(s)	The national strategy's deliberations and recommendations must be seen as benchmarks for a unified and coherent development of efforts for the benefit of people with rare diseases in both the short and long term. The strategy is not an action plan, but it contains recommendations and focus areas that can be translated into concrete initiatives.
Themes and or priorities	No themes or priorities are specifically listed within this document. However recommendations are split into chapters which are: ▪ Size and characteristics of the patient group: ○ general about the concept of rare diseases ○ occurrence. ▪ Organisation of the health professional efforts ○ special planning – principles and criteria for organisation in the hospital ○ highly specialised functions regarding rare diseases ○ status of the company at the two highly specialised centres for rare diseases ○ highly specialised dental care for rare diseases ○ rare diseases in relation to the hospitals' main and regional function level ○ general practice and rare diseases ○ the municipal health offers. ▪ Challenges for the hospital services ○ timely diagnostics ○ the need for coordination ○ adult patients ○ challenges in relation to the special planning ○ the future function of the centres. ▪ new diagnostic and treatment opportunities ○ genetics ○ screening ○ treatment. ▪ Organising rehabilitation and other initiatives in the municipality ○ the individual needs assessment ○ rehabilitation ○ municipalities' responsibility ○ the municipal health area ○ specially regarding education, education and employment in rare diseases

	○ coordination and cooperation across administrations in the municipality. ▪ New structure in the social area after evaluation of the municipal reform ○ responsibilities of the social board after the evaluation – the national coordination ○ responsibilities of the regions ○ tasks of the social board. ○ the independent consultancy in the disability field ▪ The need for coordination and coherence in the efforts. ○ user experiences ○ coordination, knowledge and cooperation across sectors ○ health agreements. ▪ Information and knowledge sharing ○ diagnosis descriptions ○ other sources of knowledge. ▪ Empowerment, patient education and patient organisations ○ empowerment and rare diseases ○ patient education ○ patient and relatives organisations ○ the umbrella organisation 'rare diagnoses' ○ other associations and organisations in the rare field ○ citizens without associations with rare conditions ○ international patient cooperation. ▪ Registries, databases and research ○ databases and registration ○ codification and classification ○ research ○ practical research in municipalities and regions. ▪ Education and competence development ○ the health area ○ the social, educational and employment area. ▪ EU initiatives in the area of rare diseases ○ initiatives and recommendations regarding rare diseases ○ EU support for the development of drugs for rare diseases – orphan medicinal products. ▪ Implementation, evaluation, follow-up and monitoring ○ implementation ○ follow-up and monitoring ○ evaluation.
Targets (if specified) and measurement method(s) (where available)	*No targets mentioned.*

Implementation action(s), lead(s) and key performance indicator(s)	No specific implementation actions are outlined however recommendations are contained within each Chapter. **<u>Size and characteristics of the patient group</u>** It is recommended to maintain the current Danish understanding, delineation and definition of the term "rare diseases" (English: rare diseases), according to which the term includes: ▪ A number of rare, mostly congenital, hereditary, complex and serious diseases and conditions that require special knowledge and expertise and that require a highly specialised, particularly well-planned, coordinated effort in the form of highly specialised diagnostics, treatment, follow-up and control together in 1-2 locations in the nursing home service. ▪ Rare diseases occur with a frequency (prevalence) of approximately 1-2 out of 10,000 or less, for example, up to approximately 500-1,000 people in Denmark. The illnesses often cannot be cured, but with relevant efforts the consequences of the illnesses can possibly be prevented, limited or treated and the patients thereby ensured a better quality of life and survival. ▪ There is no need for an absolute demarcation in Denmark, as no special rights or the like are attached to such a demarcation. ▪ As a starting point, a year-long and often multidisciplinary special be action efforts that are organised in accordance with the known special planning criteria for highly specialised functions in the hospital system. Further recommendations include: ▪ That increased attention is shown in terms of securing the necessary knowledge about the recurrence of rare disease states, including development in incidence and prevalence, development in life expectancy, etc. ▪ That a basis is ensured for the registration of rare patient groups in registries and clinical databases regarding rare diseases, and that such registers and databases are prioritised at least in line with databases within public diseases. ▪ That adequate and systematic registration of patients with rare diseases judgments are given high priority regarding quality monitoring, research and development. ▪ That an overview of existing databases and registers is established with rare diseases and that a diagnosis classification as precise and uniform as possible is used, including any by supplementary codes. **<u>Organisation of the health professional efforts</u>** No recommendations outlined. **Challenges for the hospital services** Related to referral, investigation and coordination: ▪ That there is a focus on strengthening earlier and timely diagnostics of rare diseases ▪ That opportunities are ensured for referral directly from the specialist department to other specialist departments in concretely planned coordinated investigation procedures, including the decision to refer patients who have unsuccessfully been investigated at a specialist department in a given specialty. This can be a vertical reference to a higher level of specialisation as well as a horizontal reference to another relevant specialisation. ▪ That better coordination and cooperation be developed between several specialties in relation to difficult investigation procedures, to ensure a faster and more efficient path through the system. ▪ Coordination and collaboration on a multidisciplinary basis are requirements for highly specialised functions in the hospital system, and should also be used and strengthened in relation to the diagnostic process for rare diseases.

	▪ The Centres for Rare Diseases have a special obligation to provide advice, guidance and ensure coordination when rare diseases and syndromes are suspected. This applies both to children and adults. Related to multidisciplinary treatment, follow-up and so on: ▪ There is a particular need to strengthen efforts to ensure that adult patients with rare and complex diseases with multi-organ involvement receive well-organised multidisciplinary diagnostics and treatment based on existing highly specialised functions. Special attention and strengthening of efforts for adult patients is therefore recommended. ▪ That, based on the Centres at a highly specialised level, work continues to develop models and agreements on multidisciplinary team collaboration for the patient group, so that both children and adults with a rare and complex disease are ensured a plan for relevant, multidisciplinary, interdisciplinary and well-coordinated efforts. ▪ Recognizing that complex rare diseases do not respect age, organ or specialty limits, it is recommended as a starting point that adult patients also where relevant, treated at the Centres for Rare Diseases or at the same hospital units/hospital registries where the child patients are treated, in such a collaboration that continuity and consistency over time in the patient process is ensured for the patient and a greater basis of experience, knowledge and routine is ensured for the therapists. ▪ That the patient with the rare complex disease is assigned to a well-defined medically responsible team at the highly specialised hospital with participation from, for example, the Centre for Rare Diseases, other involved special functions and relevant other professional groups. ▪ This team is in charge of coordinating the investigation and treatment process in such a way that the coordination responsibility for the process is carried out by a doctor/a medical specialist group from the Centre or from the specialty which is responsible for the investigation and treatment of the individual person's dominant problem. As this can change during the course of the illness, it may be relevant that responsibility for the course is transferred. In that case, this must be done by specific agreement in the team. ▪ That patients with a rare or suspected rare disease, congenital or suspected thought to be genetically determined, which is not placed elsewhere in the Danish Health Authority's special guidelines, can be referred to one of the two centres. The centres can ensure that the patients are assessed in the multidisciplinary team collaboration at the centre's hospital register or by follow-up visit to one of the specialty-specific highly specialised functions at the hospital. ▪ An appropriate transition from child to adult is sought, if necessary, to ensure that a decision is made early on which specialty will be responsible for the process in adulthood and that doctors and other personnel from this specialty are involved in the patient's treatment well in advance of the transition. ▪ In addition to the multidisciplinary medical effort, professionals with other special expertise should also be included, when relevant, in the multidisciplinary team collaboration between the special functions, for example, nurses, dietitians, occupational therapists, physiotherapists, psychologists, dentists and social workers. ▪ As far as possible, patient course descriptions are prepared. Here you can, among other things, the starting point is international descriptions of "best practice", for example, Gene Reviews, and the aim is to optimise knowledge building. ▪ The working group notes that, in relation to the National Board of Health's lines may be a risk that some rare patient groups cannot be "recovered" across specialties or that there may be unintentional inconsistencies in the descriptions, and therefore recommends that in the revision of the specialty plan, the focus is on ensuring consistency between the individual thesis guidance, that is, based on the strategy's considerations and recommendations. ▪ That general practice as well as the hospitals' main and regional functional levels have easy access to valid and up-to-date information regarding rare conditions and the possibility of qualified advice and sparring from the Centres for Rare Diseases and the multidisciplinary teams.

Recommendations for the medical societies:
- That the medical science companies in their business show increased attention to the special challenges that rare diseases entail. This applies in relation to specialist medical training, quality development, research etc.
- That the medical societies increase their focus on timely diagnosis and treatment, rehabilitation, research and development regarding rare conditions within the area of the individual specialisation. For example, can large specialist companies set up special committees with tasks regarding treatment of rare diseases in their area.
- That the medical societies have increased attention to and also relate to the special challenges that the "specialty homeless" rare complex illnesses entail, for example in cross-disciplinary discussions with other specialities.

New diagnostic and treatment opportunities
- That consideration be given to drawing up guidelines for the situations in which – with the advantages and disadvantages of the latest technological possibilities – it is relevant to offer a comprehensive genetic examination to a patient.
- That, in the context of the thesis plan, it should be assessed whether there is a need for collection and distribution of tasks regarding special genetic functions, including regarding collection of research and advice for selected rare diseases at fewer genetic departments.
- That it should be ensured that patients for whom a comprehensive genetic examination has not provided an explanation for the condition are given the opportunity to be re-evaluated after an appropriate period of time when relevant.
- Genetic studies should generally assume that there is a relevant clinical description/examination of the patient.

Recommendations in relation to treatment:
- Experimental treatment should be possible in relevant cases.
- Attention should be paid to the possibility of referral for research-related treatment abroad when there is a relevant opportunity for this.
- When assessing the effect of treatment modalities, emphasis is placed on including a breadth of different scientific methods and approaches.
- Patient history descriptions and treatment protocols should be prepared as far as possible fair extent based on international "best practices". International communication and cooperation between expert centres should therefore be accommodated and strengthened.
- Patient history and results of treatment trials should be documented i.e. for the purpose of knowledge building.

Organising rehabilitation and other initiatives in the municipality
- Rehabilitation for rare diseases is based on a coherent interdisciplinary assessment of the health related functional capacity and the needs for action, for examples, on the basis of the available knowledge about the disease state. Functional capacity is assessed based on the World Health Organization concept of functional capacity
- That focus is placed on the entrance to the municipality and on access to social support measures
- That fertile ground is created for interdisciplinary knowledge environments, including to ensure
- continuity and the collection of knowledge, including to a greater extent being able to gather
- expertise, so that authorities in connection with case processing have access to relevant knowledge and advice on rare diagnoses and the functional impairments that are typical for the individual diseases and disabilities
- Continuity and stability in the cooperation between families with rare diseases and their municipal case handlers and professionals is sought, including that focus is placed on the need for coordinated case handling in the municipality - preferably with one coordinating

	case handler per family, who can be the rope-bearer in relation to the various administrations and departments in the municipality and possibly the contact with the hospital system ▪ That, during the transition from child, youth and adult, it is ensured that the citizen gets the accustomed and coordinated social efforts and that particular care is taken with the transfer of knowledge, since precisely a lack of knowledge about the rare diagnoses and their manifestations can risk causing unnecessarily complicated proceedings ▪ That there is a focus on coherence and integrity in the effort, including on the healthy siblings' well-being and development opportunities. **New structure in the social area after evaluation of the municipal reform** ▪ That appropriate specialised knowledge and competences in these areas in relation to the most complicated rare disability groups/rare diseases are ensured through the National Coordination Structure. **The need for coordination and coherence in the efforts** Recommendations - Regarding the cross-sectoral effort: ▪ That there is easy access for professionals from all sectors to valid and up-to-date knowledge of rare conditions. ▪ That there is a focus on coherence in patient processes along the way through investigation, treatment, follow-up, rehabilitation and possibly palliation between the health service and the social sector. There will often be long-term lifelong parallel pre-races. ▪ That relevant information is shared across sectors, administrative areas and actors, taking into account current legislation on confidentiality and so on. ▪ That there is a focus on gathering knowledge about successful interdisciplinary and coordinated efforts between all relevant actors in the field, including the possibility of establishing new distributions of tasks and cross-disciplinary cooperation, and so on (for example, as per Batten Disease team collaboration). ▪ That continuous development of professional knowledge and competence is ensured. ▪ That regions and municipalities ensure that the health agreement covers the issues that citizens with rare diseases have in relation to coherence and high quality in rehabilitation efforts, as well as coherence in treatment and rehabilitation processes. ▪ That authorities who have to explain and make decisions about support for citizens with rare diseases are as far as possible obliged to seek out relevant knowledge and use this in case processing. **Information and knowledge sharing** Recommendations regarding information: ▪ That the diagnosis descriptions are quality assured, continued and expanded in the comments. ▪ That a mechanism for regular assessment and updating is ensured. ▪ The diagnosis descriptions incl. resources are transferred from the National Board of Health and Welfare to a platform in a strong, sustainable and robust health professional environment with the possibility of social professional input. ▪ That initiatives are taken at the relevant level regarding a realisation of this as part of the implementation of the national strategy. ▪ In addition, it is recommended in light of the ongoing EU activities in the area and opportunities and challenges in relation to the patient mobility directive, a consolidation of the Danish information effort in relation to European Union (EU) activities in the area of: ○ Danish participation in the Orphanet collaboration ○ That, in general, under the auspices of the two centres in the hospital system, work is being done towards establishing a more comprehensive overview of relevant sources of knowledge nationally and internationally.

	Empowerment, patient education and patient organisations ▪ There should be a continuous focus on empowerment when dealing with the field of rare diseases. ▪ Patient education should be an element of rehabilitation also for patients with rare diseases. ▪ Patients with rare diseases should have the opportunity to join relevant networks and participate in their activities. ▪ Special advice and support offers across the board regarding health and social problems for patients with rare diagnoses and their relatives should be developed. ▪ Voluntary associations should be involved in the work regarding the patient group's special problems, for example, as a hearing party for new legislative proposals relevant to the area, in relevant working groups etc. set up by public bodies and should be equipped to handle this task. ▪ Patient associations can be involved with great advantage in gathering experience, satisfaction investigations and so on. ▪ The rare network should continue to be an offer for rare patients and relatives who do not have the opportunity to join other relevant networks/associations. ▪ Efforts should be made to ensure that patients with rare diseases can have the opportunity for more specific patient education. **Registries, databases and research** ▪ That the RAREDIS (Nordic database for rare diseases) continues, expands and consolidates in order to achieve registration of patients with rare diseases and their patient course. The centres are thus obliged to register rare patients in the joint RAREDIS database and thereby ensure expansion and maintenance. ▪ That a basis is generally ensured for registrations of relevant rare patient groups, in registers and clinical databases in general. ▪ That an overview of existing databases and registers and so on, is established, as recommended in the Council of Ministers' recommendation, to increase knowledge about incidence as well as quality parameters in general for rare diseases. ▪ That adequate and systematic registration of patients with rare diseases is given high priority, with a view to quality monitoring, research and development. ▪ That a diagnosis classification as precise and uniform as possible is used. ▪ That, when registering patients with rare diseases, the so-called McKusick codes, better known as OMIM numbers, are still used, for example, at the centres for rare diseases and in genetics. ▪ Orphanet codes will be able to have a strength in the clinic and it is suggested that further experience regarding use of these. ▪ That greater focus is created on research into rare diseases and prioritisation of research nationally and internationally in the treatment environments, for example, via several PhD courses with the dual purpose of promoting research and recruitment of specialist doctors and nurses. ▪ That the medical societies and relevant research councils etc. be made aware of the national strategy and the perspectives regarding the international research interest in rare diseases with a view to promoting Danish and international research in the field of rare diseases. ▪ That research comes around the whole patient, from basic molecular disease mechanisms to rehabilitation and social efforts. This means that both medical, biochemical and more service- and social/psychological/pedagogically oriented subjects and personnel should be involved in the research. ▪ That Denmark participates in the Orphanet collaboration. Research recommendations: ▪ Which methods promote that more citizens with rare diseases benefit of teaching and support in childhood and adolescence.

	▪ What forms of rehabilitation, support and help, including, for example, which social work methods best compensate people with rare diagnoses, increase the person's self-determination and quality of life, and increase the person's opportunities to live a life on your own terms. ▪ What role relatives, networks and other surroundings play in relation to help and support children, young people and adults with rare diagnoses as much as possible. ▪ How the citizen/young person himself, networks and relatives, the hospital and the municipality can work together to best promote the citizen/young person's opportunities for independent living. **Education and competence development** ▪ That, with an emphasis on the general, special attention is given to rare diseases judgments in teaching at the medical school and other healthcare educations. ▪ That courses are offered for general practice regarding rare diseases, for example, in relation to Doctors' Days etc. ▪ That the medical companies in their business show increased attention to the special challenges that rare diseases entail. This applies in relation to specialist medical training and continuing education, quality development, research and so on. ▪ That the medical and nursing associations increase their focus on diagnosis, treatment, research and development regarding rare conditions within the area of the individual specialist. For example, large specialist companies can set up special committees with tasks regarding treatment of rare diseases in their area or in cross-company collaboration between companies. ▪ Development of interdisciplinary and possibly cross-sectoral teaching and training bids should be considered. Recommendations in the social area: ▪ That, in connection with the tasks of the National Board of Social Affairs and Health in relation to the National Co-ordination structure, special attention is paid to securing and re-developing specialised social work knowledge about citizens with rare diseases and functional impairments. ▪ That there is a focus on upskilling employees in the social, teaching and employment areas who work with citizens with rare diagnoses. ▪ That professional knowledge environments are built that can ensure this upskilling. ▪ That the concept of rehabilitation comes into play more in relation to citizens with rare diagnoses who have to live with the disease/disability for the rest of their lives and therefore need one "to live with" approach. ▪ The working group also recommends that educational activities generally consider the patient organisations and users - with a view to using and making useful the patients' knowledge, experiences and experiences. **EU initiatives in the area of rare diseases** ▪ That Denmark, which has followed along until now, participates and influences the work under EU auspices via the National Board of Health's professional participation in relevant forums, including, among other things, "European Commission Expert Group on Rare Diseases" and "EUnetHTA - the collaboration" just as the commitment and participation of the Patient Associations is considered positive. ▪ That regarding medicines, it is ensured that there is (continued) access to necessary ones Orphan Medicinal Products (OMP) in Denmark. **Implementation, evaluation, follow-up and monitoring** ▪ That the national strategy for rare diseases is implemented before 2018.

	▪ That a status evaluation of the strategy be prepared three to five years after preparation. The evaluation should result in a short status report.
Governance and organisational structures	The Danish Health Authority handles the secretariat function for the working group and can ad hoc supplement the working group with relevant skills, including possibly through the establishment of sub-working groups.
Funding model	No specific funding of the overall strategy mentioned. The financing of RAREDIS has been based on grants from private funds, despite the Danish Health Authority's recommendation and approval as a clinical quality database. Stable, lasting funding is therefore an important prerequisite for further expansion and development of the database.
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	*Yes, see chapter New Diagnostic and Treatment Options – section Screening. Screening is further mentioned within the Centres of Expertise.*
Personalised medicine, genomics, genetic counselling	*Yes, see chapter New Diagnostic and Treatment Options – section Genetics and associated recommendations (see implementation actions).*
Models of care/care pathways	*Yes, throughout however more specific instances include chapters Organisation of the Health Professionals Efforts Organising Rehabilitation and Other Initiatives in the Municipality.*
Workforce	*See Chapter – Education and Competence Development and associated recommendations (see implementation actions).*
European Reference Networks	Yes, mentioned in Chapter – EU initiatives in the field of rare diseases and recommendation: That Denmark, which has followed along until now, participates and influences the work under EU auspices via the National Board of Health's professional participation in relevant forums, including, among other things, "European Commission Expert Group on Rare Diseases" and "EUnetHTA - the collaboration" just as the commitment and participation of the Patient Associations is considered positive.
EU alignment and participation	In 2009, Denmark joined this recommendation from the EU's Council of Ministers on measures regarding rare diseases, including that all countries should have a formulated national strategy/action plan for rare diseases no later than 2013. The recommendation came as a follow-up to an earlier announcement from the EU Commission. The prescription from 2009 focuses broadly on a number of areas for rare diseases and patients with rare diseases, that is, research, diagnosis, access to treatment, empowerment of patients and their organisations as well as cross-sector and international cooperation.
Health information (including rare disease registries)	*Yes, see Chapter Registries, Databases and Research and Chapter Information and Knowledge Sharing along with associated recommendations (see implementation actions).*

Orphan medicines	See Chapter – EU initiatives in the field of rare diseases – segment EU support for the development of medicines for rare diseases – orphan medicinal products. A specific recommendation is: ▪ That regarding medicines, it is ensured that there is (continued) access to necessary ones OMP in Denmark.
Rare disease research	*Yes, see Chapter Registries, Databases and Research.*
Alignment beyond the healthcare sector	*Yes see Chapter Organisation of rehabilitation and other initiatives in the municipality. Specific areas referred to are social, teaching and training and employment. Also observed in Chapter The need for coordination and coherence in effort.*
Any additional information (for example, background to the strategy or strategy development)	**<u>Working group</u>** In light of the recommendation from the Council of Ministers and the development since the report in 2001, there was a need to review, evaluate and update the recommendations in the area, for example, taking into account the European perspective and the recommendations for a national strategy that appear in the Council of Ministers' recommendation. The Danish Health Authority, in agreement with the Ministry of Health and Prevention, therefore set up a broad working group with a view to preparing updated recommendations in the area. Based on the Danish Health Authority's statement regarding rare disabilities 2001 and the Council of Ministers' recommendation and recommendations, the working group was tasked with describing and assessing: ▪ The size and special characteristics of the patient groups ▪ The needs for efforts in relation to diagnostics, treatment, care and control as well as ▪ Rehabilitation ▪ The current organisation of offers, including the cooperation between sectors, based on patient progress ▪ The needs for experience and knowledge gathering, documentation and research ▪ The needs for information and knowledge dissemination ▪ International cooperation. Representation on the working group includes: The National Board of Health; Ministry of Health and Prevention; Capital Region; Region Zealand; South Denmark Region; Central Jutland region; The National Association of Municipalities; Danish Paediatric Society; Rare Diagnoses; The Kennedy Centre. For full list of working group members see document. **<u>The work of the working group</u>** The working group has held a number of meetings with the aim of discussing relevant areas for a national strategy for rare diseases. In relation to this, all members of the working group presented presentations on problems and challenges seen from their point of view and hinterland. Following this review, the drafting of the national strategy began. In relation to this, the working group decided to set up a sub-working group with the task of carrying out a review and assessment of the so-called diagnosis descriptions, as well as considering the possibilities for securing continuously available and updated Danish language information on rare diseases.

	The working group finds that the purpose of the strategy, that is, to further elevate the area of rare diseases, including developing the area and adjusting the previous strategy on the basis of the experience gained and the general development that has taken place since 2001 in the relevant areas, including, among other things, the specialist planning established in the legislation, the municipal reform from 2007 and the results of the evaluation thereof in the autumn of 2013. The previously used term "rare disabilities" has generally been replaced in the healthcare system by "rare diseases", i.e. on the basis of the international term "rare diseases". In other contexts, the term "rare disabilities" is still often used. And the patient organisations use the term: "rare diagnoses". However, all three designations cover the same conceptual and definitional boundaries. Correspondingly, in the respective sections, the words patient, user or citizen are used in slightly varying ways for persons with rare diseases. This reflects, that is, the different culture and approach in the respective sectors. The working group has found it most appropriate to maintain this variation.

Key: EU: European Union; OMP: Orphan Medicinal Products; RAREDIS: Nordic database for rare diseases.

Note: The information in this table was extracted from a version of the original document translated to English using Google Translate.

Table B7. Data extracted for Denmark (2018 evaluation)

Denmark	Strategy information
Author(s) **Title**	The Danish Health Authority National strategy for rare diseases: Status evaluation and recommendations for future efforts[25]
Timeline	Published in 2018.
Overall aim(s)	The purpose of the status evaluation is to take stock of the National Strategy for Rare Diseases in Denmark (National Health Authority, 2014), and on the basis of uncovering the challenges, come with recommendations that can help to remedy them and support the quality of future efforts. Three to five years after initial strategy publication this report provides the status of the implementation of the strategy's approximate 100 recommendations, and results in an action-oriented status report that focuses on selected topics and recommendations. In the preparation for the status evaluation, based on the strategy's chapters, it has been found appropriate to condense the 100 recommendations into six selected themes, which together cover the majority of the strategy's recommendations.
Themes and or priorities	The six selected themes in this review are: 1. Rare patients in the hospital system and in the municipality 2. Sector transitions, cooperation and coordination 3. Patient involvement, coping and empowerment 4. International cooperation 5. Education and skills 6. Registration, documentation and knowledge.
Targets (if specified) and measurement method(s) (where available)	*None mentioned.*
Implementation action(s), lead(s) and key performance indicator(s)	***Theme 1: Rare patients in the hospital system and in the municipality*** **<u>Recommendations regarding implementation and continued dialogue:</u>** **The Danish Health Authority recommends:** 1. That the Danish Health Authority holds an annual status meeting for the next three years with the parties involved to ensure implementation of the recommendations and continued dialogue in the area. **<u>Recommendations regarding rare patients in the hospital system and communities:</u>** **The Danish Health Authority recommends:** *Correct visitation* 2. The Danish Health Authority, with the involvement of the regions and centres for rare diseases, will initiate a process that clarifies the individual specialist guidelines in relation to the treatment of rare diseases, creates consistency between the specialist guidelines and ensures an appropriate organisation.

	3. The centres for rare diseases jointly and with the involvement of relevant parties draw up referral guidelines for how young and adult patients can enter the centres for rare diseases and for who can appropriately stay/not stay in the centres. The referral guidelines must take into account the speciality plan. *Diagnostics at the highest level* 4. Cooperation between clinical genetics departments, the centres for rare diseases and paediatric departments under regional auspices is strengthened and developed throughout the diagnostic process, including to ensure that new diagnostic methods are used for follow-up and diagnosis of patients who have not previously received a molecular genetic diagnosis. 5. The genetic investigation and diagnostics are carried out under the auspices of the clinical genetic departments in order to ensure that the most suitable diagnostic methods are used and that the interpretation and dissemination of analysis results is carried out by professionals with clinical genetic specialist knowledge. *Coherent patient course for children, young people and adults* 6. The centres for rare diseases must: (a) ensure an appropriate transition from child to adult. Below that guidelines are drawn up for how young and adult patients who need this can stay at the centres for rare diseases and for how the transition to other specialties is ensured for young people and adults who do not have to stay in the centres for rare diseases. (b) develop models and agreements on multidisciplinary teamwork, so that both children, young people and adults with a rare and complex disease are ensured a multidisciplinary, interdisciplinary and well-coordinated effort regardless of place of residence. (c) prepare patient course descriptions for the major rare diseases, based on national and international descriptions of "best practice". (d) upgrade support functions, including psychological assistance, social worker assistance and physiotherapy depending on the local conditions. *Advise and disseminate knowledge to patients and relatives, healthcare staff and municipalities* 7. The Centres for Rare Diseases and the National Knowledge and Special Advisory Organisation must ensure easy access for professionals from all sectors to valid, user-friendly and up-to-date knowledge about rare diseases. **Recommendations regarding municipalities:** *Correct visitation and coherent patient process for children, young people and adults* 8. The municipalities ensure holistically oriented and coherent process, for example, through work with: (a) establishment of one entrance and exit to/from the municipality. (b) one coordinating case manager who can ensure coordination and handover of information between case managers, doctors and municipal specialist staff and so on, as well as guide the citizen and contribute to minimising the number of contacts in the citizen process. *(c)* cross-cutting teams with a view to strengthening coordination across professional and administrative areas in cases with high complexity. This assumes that the citizen gives consent to the exchange of information. (d) creation of municipal networks across the country with a view to mutual learning and inspiration and uniform management of offers in the country. *Advise and disseminate knowledge to patients and relatives, healthcare staff and municipalities* (e) that municipalities with experience in coordinating courses for citizens with rare diseases in collaboration with the social services make their knowledge and experience available to the staff at centres for rare diseases, for example, through joint knowledge-sharing activities.

	Theme 2: Sector transitions, cooperation and coordination **Recommendations regarding sector transitions, cooperation and coordination:** **The Danish Health Authority recommends that:** 9. The centres for rare diseases strengthen course coordination, coherence and overview in the often very complex treatment processes for example by strengthened use of functions such as the doctor responsible for the patient and the process coordinator function. This applies both to cooperation and the handing over of information between relevant hospital departments and across sectors. 10. The centres for rare diseases and the municipalities exchange patient information, and mutual access to contact regarding the individual patient is ensured between the process managers in the respective municipality and centres for rare diseases and access for the municipalities to the medical expertise in the centres for rare diagnoses. 11. Regions and municipalities in their collaboration consider rare disease cases. This can be done, for example, by drawing up specific agreements for the rare target group, or by including the rare target group in general health agreements, where patient processes cross regions, municipalities and general practice. 12. The National Board of Social Affairs and Health, through the national coordination structure, follows the development of target groups, offers and initiatives in the most specialised social and special education area, and collects and disseminates knowledge about these, including publication of course description(s), for selected target groups. ***Theme 3: Patient education, coping and empowerment*** **Recommendations regarding patient education, coping and empowerment:** **The Danish Health Authority recommends that:** 13. Regions, municipalities and patient organisations maintain and strengthen the citizens' and relatives' ability to cope, etc. to ensure optimal treatment results, increased quality of life and prevent social isolation, including: (a) The patient organisations in collaboration with regions/centres for rare diseases and municipalities develop offers for patient education at themed evenings, collaboration with voluntary organisations and virtual course material. The offers can be targeted at specific subgroups, including children, young people, adults, people with developmental disabilities or Danes with other ethnic backgrounds. (b) Initiate projects that aim to test/adjust/spread existing general models for other patient groups in need of help, so that they can also be applied to people with rare diseases. 14. Patient organisations prepare/update information material with citizen oriented knowledge and information about rare diseases, offers for support for coping, and so on, with the involvement of professionals. 15. Counselling services to promote patient empowerment, also going forward, must be services for people with rare diseases and their relatives. ***Theme 4: International cooperation*** **Recommendations regarding international cooperation:** **The Danish Health Authority recommends that:** 16. The regions are building a national cooperation with respect to Danish delta participation in international cooperation, including Danish participation in the European Reference Network and Orphanet. 17. The regions build regional networks that support coordination of the regions' work between Danish European Reference Network members, including the application process for the hospitals and contribute to the regional dissemination of relevant information from the Danish Health Authority.

	18. The Danish Health Authority supports the regions in the above and strengthens Danish participation in the European Reference Network by, in the build-up phase, to: (a) clarify that hospitals with highly specialised functions are recommended to be part of the European Reference Network, if relevant networks exist (b) support the integration of Danish hospitals into international collaborations by mediating contact and providing information, for example, by holding an information meeting when the next application deadline is known (c) participate in Nordic cooperation, including Nordic Network on Rare Diseases and Nordic Cooperation on Highly Specialised Treatment and Clinical Trials, where cooperation opportunities in relation to the European Reference Network are discussed. ***Theme 5: Education and skills*** **Recommendations regarding education and skills:** **The Danish Health Authority recommends that:** 19. The teaching effort is strengthened, primarily in specialist medical training in relation to diagnosis and treatment in rare diseases, and so on, that all specialties in their target descriptions indicate learning competencies with a focus on the specialist being able to see symptoms as a possible part of a major complex rare disease so that relevant patients can be examined for investigation in the centres for rare diseases. 20. Relevant medical scientific societies prepare a description of how an expert training/further training regarding rare diseases can be composed. 21. It is being investigated how diagnostic descriptions for rare diseases can be anchored and expanded in the future in the Medical Handbook. 22. The necessary skills of other health personnel who deal with patients with rare diseases are strengthened. **Theme 6: Registration, documentation and knowledge** **Recommendations regarding registration, documentation and research:** **The Danish Health Authority recommends that:** 23. The regions and the Centres for Rare Diseases jointly: (a) consolidate and expand the RAREDIS database nationally so that all relevant patients are included and strengthen the ongoing registration of rare diagnoses at the clinical genetic departments (b) ensure uniformly comprehensive registration practices, for example, by using explicit codes that enable the identification of rare diseases (c) map existing databases and registers and their reversal option, for example, with a view to integration in RAREDIS in collaboration with the regions' clinical quality development programme (d) strengthen research that includes patient processes both inside and outside hospital.
Governance and organisational structures	The Danish Health Authority has handled the secretariat function, and the status evaluation has been prepared in collaboration with the National Board of Social Services. During the work, advice was received from the follow-up group.
Funding model	There is no associated funding for the national strategy. Current expenditure for rare diseases, as for all other diseases, is within the general health system budget of the regions and municipalities.

	There is no dedicated funding allocated for the activities in the national strategy. But funding for National Strategy activities is incorporated into the general budget.
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	National neonatal screening schemes are in place for phenylketonuria, congenital hypothyroidism, congenital adrenal hyperplasia, maple syrup urine disease, argininosuccinate lyase deficiency, carnitine transporter defect, medium chain acyl-CoA dehydrogenase deficiency, long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency, very long chain acyl-coA dehydrogenase deficiency, glutaric acidaemia type 1, methyl malonic acidaemia, propionic acidaemia, multiple carboxylase defect, argininosuccinic aciduria, tyrosinaemia type 1 and biotinidase defect. Since 2016, newborns are also tested for cystic fibrosis. The timing for drawing the blood samples (done by heel-prick) is within 48-72 hours following birth, allowing for earlier intervention and treatment. Neonatal hearing screening is also part of the national policy.
Personalised medicine, genomics, genetic counselling	*See recommendations in Theme 1.* Genetic testing is performed in departments of clinical genetics in all regions of Denmark. In addition genetic testing is also carried out in a few clinical biochemical departments. Diagnostic tests in Denmark are made for more than 500 genes and more than 500 diseases in the Orphanet database. Next-generation sequencing /exome sequencing is now available in Denmark. Genetic testing for medical reasons is part of the national healthcare system and free of charge. Genetic testing abroad is possible mediated by the departments of clinical genetics. State reimbursement of costs for tests abroad can be effected after approval from the Danish Health Authority.
Models of care/care pathways	*Yes, see Theme 1: Rare patients in the hospital system and in the municipality.*
Workforce	*See Theme 5: Education and skills.* **Training and Education** In our national strategy for Rare diseases (2014) a list of initiatives is made, but so far no new initiatives have been carried out. The two Rare Diseases Centres participate in educational activities for nurses and doctors. Furthermore, they provide teaching for other healthcare professionals, families, teachers and caretakers. Master's degree in medicine at the University of Southern Denmark is under review. In addition to the joint training (for all medical students) it will be possible for medical students to have a stay at the Clinical Genetics Department, where the focus will be on genetics and counselling and diagnosing patients with rare diseases. The medical specialist education in clinical genetics has recently been revised with targeted focus on knowledge and systematic training in rare diseases. Thus, specialists in handling specific patient cases and participation in courses, obtain skills in examination and diagnosis of rare diseases and mastery of interdisciplinary collaboration with other specialties.
European Reference Networks	*Yes, see Theme 4: International Cooperation*. Denmark has a formal process in place for endorsing Health Care Providers to participate as members or coordinators of a European Reference Network (ERN).

	Denmark does not know if there are national Health Care Providers participating as member or coordinators of an ERN. All Danish applications sent to the Danish Medicines Agency (DMA) have been coordinated by representatives from other member states; however this is not clearly stated in the applications sent to the DMA. There are for the time being no established networks within the ERN, as the assessment process in the EU has only just begun. The DMA has received 23 applications for national endorsement. The level of participation is not stated in the applications.
EU alignment and participation	*Yes, see Theme 4: International Cooperation.* The national strategy measures use a different definition than the EU.
Health information (including rare disease registries)	*Yes, See Theme 6: Registration, documentation and knowledge.* No single centralised register for rare diseases currently exists in Denmark, but a number of different registries and biobanks exist although there is currently no public register giving an overview of the existing registries and biobanks dealing with rare diseases. The Serum Institute has hosted the registry and biobank of all newborn screening blood samples since 1980. The Kennedy Centre maintains biobanks on specific rare disorders such as Menkes disease and various genetic eye diseases. All visually handicapped children are registered until the age of 18. Furthermore, several research departments have registries of rare disease patients. The RAREDIS database which collects clinical data has been developed in Denmark in accordance with the recommendations in the Danish report of rare diseases from 2001 and has been in function since 2007 at the two Centres of Rare Diseases in Denmark. For the moment a few other departments can also report to the data base. It is planned that all the departments of clinical genetics in Denmark will get admission to report to the database in the future. Centres of rare diseases in the Nordic countries use their local version of RAREDIS for collecting clinical data. The information collected here can be used for research projects and bench marking at a Nordic level for different rare diseases. The Danish National Patient Registry exists since 1977 and collects systematic information on diagnoses, surgical treatment, and various demographic parameters on all patients admitted to hospital or similar institutions in Denmark. The Danish personal identity numbers give possibilities to follow up patients through the years and combine data with other national registries such as the cancer registry, registry for cause of death and so on, and to clinical databases and more specific registries. Danish teams contribute to some European registries such as the European cystic fibrosis registry; the European registry and network for Intoxication type Metabolic Diseases; the European Malignant Hyperthermia Group; and the European network of population-based registries for the epidemiological surveillance of congenital anomalies. There is also currently a helpline in place dedicated to rare diseases. Within the framework of a four-year project, Rare Diseases Denmark opened a Helpline by October 1 2016. The Helpline is operated by professionals and volunteers, who are capable of supporting people living with rare disease with information, guidance and counselling via phone and e-mail. The Helpline team is supported by a group of experts. The Helpline is located in the secretariat of Rare Diseases Denmark (RDD) and the opening hours are similar to the opening hours of the secretariat plus three hours, all in all 22 hours per week. The estimated number of inquiries is 200 – 400 per year. The RDD Helpline has applied for membership of the European Network of Rare Disease Helpline.
Orphan medicines	75 Orphan Medicinal Products (OMPs) are marketed in Denmark. Out of 91 orphan medicinal products with an EU market authorisation, 75 are approved in Denmark and are on the Danish national formulary of medicines. The remaining 16 are approved but not on the Danish national formulary of medicines. No distinction is made in Denmark as to whether the medicinal product is intended for the treatment of

	rare diseases or not. Special publication lists are not prepared. Lists of currently available marketed products (including orphans) are updated every two weeks and can be accessed here: medicinpriser.dk. No incentives are provided at present to support research into and the development of OMPs. As for other disease states and where there is a medical need, the compassionate use programme can be availed of for rare diseases. Compassionate use is not new in Denmark.
Rare disease research	*Yes, See Theme 6: Registration, documentation and knowledge.* Denmark has no specific programmes/projects to fund/facilitate rare disease research. At the moment there are no plans to conduct social or social-economic research. There are no specific programmes or calls/grants dedicated to rare diseases research in Denmark. Although there are no specific initiatives to support research into rare diseases in Denmark, Danish researchers are active in the field and there are resources in place (biobanks, registries, databases) for rare disease research.
Alignment beyond the healthcare sector	Specific actions exist to enable real access for people with rare diseases to general social/disability programmes (that is, training, guidelines for social workers and so on).
Any additional information (for example, background to the strategy or strategy development)	**Strategy evaluation:** There is a multi-stakeholder (including patients) group and is functioning (irregular meetings and activities). Status evaluation is undertaken by the Danish Health Authority in collaboration with the National Board of Social Services and will subsequently serve as a status report for the work on rare diseases in Denmark. The status evaluation was initiated in autumn 2016 with a collection of contributions from the parties who formed the original working group for the preparation of the national strategy. The contributions were used at an initial status meeting at the Danish Health Authority on 26 October 2016, where the same parties were invited. Composition of the group: Phenylketonuria Association, Rare Diseases Denmark, Danish Regions, Local Government Denmark, National Board of Social Services, Danish Health Authority, Ministry of Health, Danish Paediatric Society, Danish Society of Medical Genetics, The Danish College of General Practitioners, Organisation of Danish Medical Societies, The Capital Region of Denmark, Region Zealand, The Region of Southern Denmark, Central Denmark Region, The North Denmark Region. On the basis of the status meeting, the Danish Health Authority prepared a memorandum that described the Danish Health Authority's and the National Board of Social Services' proposal for work process, delimitation of subjects and proposals for possible new recommendations. The follow-up group commented and qualified the proposals. The Danish Health Authority, the National Board of Social Affairs and Rare Diagnoses then selected the 4 themes that were further worked on at the EUROPLAN workshop in the House of Handicap Organisations on 17 November 2017, and which also form the main focus of the current status evaluation. The report contains a concise description of some significant challenges in the rare area, as well as the participants' wishes and recommendations within the selected themes. The selected recommendations have again been discussed and qualified at a final meeting of the follow-up group on 20 June 2018, just as a revised draft of the report has then been sent to the follow-up group for comment. **Status of the national strategy** Since the strategy was published, significant progress has been made in a number of areas. There has been a breakthrough especially in the genetic diagnostic area, where new gene analyses are increasingly used as part of clinical everyday life when it comes to diagnostics of rare diseases. This development is expected to continue apace in the coming years. Early genetic examinations are important in order to

	get the patients referred to relevant specialists, so that they can be helped in the best possible way, just as the long examination procedures can in some cases be avoided. A number of other measures have also taken place in the health and social sector since 2014. A revised specialist plan has been introduced, in which a number of specialist functions have been defined in relation to rare diseases across several specialisations. However, there are still a number of cut-off problems that relate to the special plan. For example, there are still a number of rare diseases that are not mentioned in the relevant specialist guide(s). In addition, there is not always full agreement between the specialist guides, which is expressed by the fact that a rare disease can be mentioned in one specialist guide, but not in another of the relevant specialist guides. A problem in this context is that the care of certain rare diseases is stipulated as a highly specialised function in the specialist guidance for paediatrics, but not in the relevant organ-specific specialist guidance(s), which cover the care of adult patients with the same disease. With relevance to the treatment of adult patients with rare diseases in the hospital system, it can also be pointed out that there is still a challenge in ensuring a good transition from child to adult - not least in cases where the adult has to transfer from the centres for rare diseases for treatment in one or more organ-specific specialties. In the area of social and special education, the National Coordination Structure has been introduced to ensure the necessary supply of highly specialised interventions and offers for people in the most specialised social and special education area. The National Board of Social Affairs and Health, under the auspices of the National Coordination Structure, has prepared a course description for children and young people with rare disabilities, which is a set of recommendations at national level on how courses are organised in the social and special education areas. It also describes interfaces and cooperation between the actors in these areas and the health sector, including the two centres for rare diseases in Aarhus and Copenhagen respectively. In 2017, a medicine council was established which, among other things, evaluates new medicines in relation to effect, existing treatment and price. Rare diseases are explicit mentioned in the Ministry of Health's principle paper on prioritisation of hospital medicines, and work is being done on an appropriate model for how the regions make decisions about taking new medicines for rare diseases into use. The umbrella organisation Sjældne Diagnoser has opened a Helpline as a free and anonymous support and advice offer for people with rare diseases and their relatives. As a new initiative, funds have been allocated in the rate pool agreement in the social area for 2018 to test models for one coordinating case manager in the child disability area, and the project is expected to be completed in 2021. Work continues with the systematic registration of patients with rare diseases under the auspices of RAREDIS at the Centres for Rare Diseases, the majority of the country's genetic departments and the other departments associated with the database. Systematic registration of the treatment of patients with rare diseases is essential in order to ensure the quality of the current treatment and to build up knowledge about the effect of interventions, to optimise the treatment and to obtain accurate prevalence figures. Furthermore, there have been a number of European initiatives in the area – including the State of the Art publication, which provides an overview of activities relating to rare diseases in the EU and the individual EU member states, just as ERNs have been established, which basically have for the purpose of structuring cooperation between professionals across countries. **Continued Challenges** Despite the fact that since the publication of the national strategy, a number of advances have been made, overall a number of the same challenges that the national strategy identified in 2014 still exist.

	A number of challenges related to the treatment of patients with rare diseases in the hospital system are pointed out. What these have in common is that they largely have to do with ensuring consistency for patients and coordination across the hospital system and sectors. In the hospital system, the interface problem relates, as mentioned, to the Danish Health Authority's specialty plan, which does not fully solve or cannot solve the interface problems between the centres for rare diseases at Aarhus University Hospital and Rigshospital, respectively, and the other relevant hospital departments. There is thus a challenge in creating greater clarity about the target group for the centres for rare diseases. Including in relation to adult patients, as well as implementing the "collection mechanism" which is formulated in the strategy and which must contribute to fewer patients with rare diagnoses falling between two stools. The collection mechanism means that patients with rare diseases who are not clearly placed elsewhere in the specialty plan can be referred to the centres for rare diseases. If the patient needs the centres for rare diseases is assessed to be outside the centre's area of competence, the patient is referred to the relevant specialist. The transition from child to adult presents a special challenge. This happens when patients transfer from one of the two centres for rare diseases to the relevant organ-specific specialty (the adult specialty) in connection with the transition from child to adult. Especially for adult patients who are cared for in an organ-specific specialty, it can be a challenge to ensure the broad interdisciplinary and multidisciplinary approach that patients with rare diseases often need. It is also still a general challenge that patients with rare diseases are not always treated by the relevant specialists, and that there is a lack of specific knowledge about their disease in many places in the hospital system. Irrespective of which organisational model is pointed to for handling the transition, it will often be of great importance that the centres for rare diseases continue to play a role in the patients' process. The challenge regarding the coordination between sectors and internally in the municipalities is due, among other things, to the fact that patients with rare diseases often need both a healthcare effort in the hospital system and a municipal effort at the same time. For example, in the form of care or a coherent rehabilitation effort involving efforts in the municipality in the areas of health, social care, education and employment. Parents of children with disabilities may find that the efforts they receive in both sectors are disjointed and uncoordinated. Empowerment is a central concept in relation to the treatment and rehabilitation of people with rare diseases and disabilities. It is considered relevant that all sectors work to strengthen empowerment and the rehabilitation mind set physically, psychologically and socially in relation to people with rare diseases, so that all efforts are based on the overall need. The goal is for the person with the rare disease to be able to live with the disease and the resulting functional impairments as best as possible. There is still considered to be a need to generally raise the level of knowledge about rare diseases, for example, through available professional articles, events, and so on, for people with rare diseases, their relatives and relevant professionals. Including dissemination of knowledge about existing offers under the auspices of civil society such as Helpline, the Rare network and rare navigators. In the field of rare diseases, international cooperation across national borders is associated with great value, because the number of professionals with specialised knowledge is few. There is cooperation both on a Nordic, European and multinational level (World Health Organization). It can be difficult to form an overall overview of the activities. In this context, the follow-up group has chosen to have a special focus on the ERN, which are virtual networks involving healthcare providers across Europe. The purpose of the ERN is basically to structure the collaboration between professionals across countries. The purpose of these networks is thus to tackle complex or rare

	diseases or disorders that require highly specialised treatment and concentration of knowledge and resources. The first ERNs were fully established in 2017. It is extensive to apply for admission to the ERN, and the professional environments find that they need support in connection with the application process There is generally a perceived need to strengthen the teaching efforts in specialist medical education, at medical school and other health science education and further education in relation to diagnosis, treatment and research in rare diseases. It is not necessarily specific knowledge about concrete rare diseases that needs to be strengthened, but rather that all specialties in their education programmes and plans relate to rare diseases, including that the specialty-specific symptom or disease they see can be part of a larger and more complex disease. There is no comprehensive registration of all patients with rare diseases, and the registration can often be incomplete. This is due, among other things, to the fact that only a small number of rare diagnoses have a specific ICD-10 code. Under the auspices of the European Joint Action on Rare Diseases, committee work is underway, which will result in a pan-European diagnosis and code classification system. There is a challenge in relation to defining which rare diseases and genetic abnormalities should be registered in RAREDIS. This is due, among other things, to the fact that there have been many new genetic studies where the result is not unambiguous or other conditions that make the result difficult to interpret. It is a continuing challenge to ensure sufficient research, among other things, because there are so few patients and because there is a lack of systematic registration.

Key: DMA: Danish Medicines Agency; ERN: European Reference Network; EU: European Union; OMP: Orphan Medicinal Product; RAREDIS: Nordic database for rare diseases; RDD: Rare Diseases Denmark.

Note: The information in this table was extracted from a version of the original document translated to English using Google Translate.

Table B8. Data extracted for Denmark (2022 evaluation)

Denmark	Strategy information
Author(s) **Title**	Marselisborg Consulting Evaluation of the National Strategy for Rare Diseases[26]
Timeline	Published December 2022
Overall aim(s)	This report conveys an evaluation of the national strategy from 2014 as well as the Status evaluation of the National Strategy for Rare Diseases. The purpose is to collect and disseminate results and experiences from the work with the national strategy with a view to providing a renewed overview of the area and with a particular focus on increasing the quality of the organization around rare diseases going forward.
Themes and or priorities	Theme 1: Rare patients in the hospital system and the municipality Theme 2: Sector transitions, cooperation and coordination Theme 3: Patient education, coping and empowerment Theme 4: International cooperation Theme 5: Education and skills Theme 6: Registration, documentation and knowledge Theme 7: Availability of treatment Theme 8: Implementation Cross-cutting focus areas relevant to further work: ▪ A cross-cutting look at the need for competencies ○ Need for specialised skills ○ Need for broad knowledge about the management of rare diseases ○ Routine arises from meeting people with a rare disease. ▪ Need for clarity around finances in order to maintain competencies ○ Economy is a significant factor ○ The area is more vulnerable to temporary funding. ▪ The importance of a rigorous focus from all parts of the healthcare system ○ The municipal area is under pressure, and it affects the rare area ○ Need to focus on a targeted municipal effort. ▪ Need to support the development of medicine and treatment in small groups ○ Great development despite the strategy's lack of focus ○ The rarity challenges the normal processes and market forces. ▪ Focus on relatives and the network around the person with the rare disease ○ Relatives need focus – but how? ○ Good experiences from, for example, the municipal effort

Targets (if specified) and measurement method(s) (where available)

Illustration 1: The three evaluation perspectives and the assessment based on them

Evaluation perspective	For each recommendation, an assessment is made as to whether it...
Implementation	... has largely been implemented
	... has been implemented to some extent, but attention is still outstanding
	... has been implemented to a low degree or not at all
Impact	... has largely had a positive effect on the patients
	... to some extent has had a positive effect on the patients
	... has had little or no positive effect on the patients
Relevance	... to a large extent is still relevant in relation to the problem, so the effort must be continued
	... is to some extent relevant to the challenge, and the area should continue to have focus, albeit in an adjusted form
	...continues to have relevance to a low degree or not at all

Note: In the table below, these ratings are extracted numerically, as follows:

1. *Green symbols – largely implemented;, largely positive impact; largely still relevant*
2. *Yellow symbols – implemented to some extent; some positive impact; some relevance albeit adjusted*
3. *Red symbols – little to no implementation; little to no positive impact; little to no relevance*

Implementation action(s), lead(s) and key performance indicator(s)

Recommendation	Implementation	Impact	Relevance
Theme 1: Rare patients in the hospital system and the municipality			
Recommendation 2: The Danish Health Authority, with the involvement of the regions and centres for rare diseases, will initiate a process that clarifies the individual specialist guidelines in relation to the treatment of rare diseases, creates	2	1	1

	consistency between the specialist guidelines and ensures an appropriate organisation.			
	Recommendation 3: The centres for rare diseases jointly and with the involvement of relevant parties draw up referral guidelines for how young and adult patients can enter the centres for rare diseases and for who can appropriately stay/not stay in the centres. The referral guidelines must take into account the speciality plan.	3	3	1
	Recommendation 4: Cooperation between clinical genetics departments, the centres for rare diseases and paediatric departments under regional auspices is strengthened and developed throughout the diagnostic process, including to ensure that new diagnostic methods are used for follow-up and diagnosis of patients who have not previously received a molecular genetic diagnosis.	2	2	3
	Recommendation 5: The genetic investigation and diagnostics are carried out under the auspices of the clinical genetic departments in order to ensure that the most suitable diagnostic methods are used and that the interpretation and dissemination of analysis results is carried out by professionals with clinical genetic specialist knowledge.	2	1	1
	Recommendation 6: The centres for rare diseases must: a) ensure an appropriate transition from child to adult. Below that guidelines are drawn up for how young and adult patients who need this can stay at the centres for rare diseases and for how the transition to other specialties is ensured for young people and adults who do not have to stay in the centres for rare diseases b) develop models and agreements on multidisciplinary teamwork, so that both children, young people and adults with a rare and complex disease are ensured a multidisciplinary, interdisciplinary and well-coordinated effort regardless of place of residence c) prepare patient course descriptions for the major rare diseases, based on national and international descriptions of "best practice" d) upgrade support functions, including psychological assistance, social worker assistance and physiotherapy depending on the local conditions.	2	2	1
	Recommendation 7: The Centres for Rare Diseases and the National Knowledge and Special Advisory Organisation must ensure easy access for professionals from all sectors to valid, user-friendly and up-to-date knowledge about rare diseases.	1	2	3
	Recommendation 8: The municipalities ensure holistically oriented and coherent process, for example, through work with: a) establishment of one entrance and exit to and from the municipality. b) one coordinating case manager who can ensure coordination and handover of information between case managers, doctors and municipal specialist staff etc. as well as guide the citizen and contribute to minimizing the number of contacts in the citizen process.	3	3	1

	c) cross-cutting teams with a view to strengthening coordination across professional and administrative areas in cases with high complexity. This assumes that the citizen gives consent to the exchange of information. d) creation of municipal networks across the country with a view to mutual learning and inspiration and uniform management of offers in the country. e) that municipalities with experience in coordinating courses for citizens with rare diseases in collaboration with the social services make their knowledge and experience available to the staff at centres for rare diseases, for example, through joint knowledge-sharing activities.			
	Theme 2: Sector transitions, cooperation and coordination			
	Recommendation 9: The centres for rare diseases strengthen course coordination, coherence and overview in the often very complex treatment courses, for example by strengthened use of functions such as the doctor responsible for the patient and the course coordinator function. This applies both to cooperation and the handing over of information between relevant hospital departments and across sectors.	1	1	2
	Recommendation 10: The Centres for Rare Diseases and the municipalities exchange patient data, and reciprocal access to contact about the individual patient is ensured between the course managers in the municipality and the Centre for Rare Diseases, respectively, and access for the municipalities to the medical expertise in rare diagnosis centres.	1	1	1
	Recommendation 11: Regions and municipalities in their collaboration consider rare diseases. This can be done, for example, by drawing up concrete agreements for the rare target group, or by including the rare target group in general health agreements, where patient processes cross regions, municipalities and general practice.	3	3	2
	Recommendation 12: The National Board of Social Affairs and Health, through the national coordination structure, follows the development of target groups, offers and efforts in the most specialised social and special education areas, and collects and disseminates knowledge about these, including publication of course description(s) for selected target groups.	2	3	1
	Theme 3: Patient education, coping and empowerment			
	Recommendation 13: Regions, municipalities and patient organisations maintain and strengthen citizens' and relatives' ability to cope with to ensure optimal treatment results, increased quality of life and prevent social isolation, including: a) The patient organisations in collaboration with regions/Centres for Rare Diseases and municipalities develop offers for patient education at themed evenings, collaboration with voluntary organisations and virtual course material. The offers can be targeted at specific subgroups, including children, young people, adults, people with developmental disabilities or Danes with a different ethnic background.	2	1	1

b) Initiate projects that aim to test/adjust/spread existing general models for other patient groups in need of help, so that they can also be applied to people with rare diseases.				
Recommendation 14: Patient organisations prepare/update information material with citizen-oriented knowledge and information about rare diseases, offers of support for coping, and so on, with the involvement of professionals.	2	2	1
Recommendation 15: Counselling services to promote patient empowerment must also be offered to people with rare diseases and their relatives in the future.	1	1	1
Theme 4: International cooperation			
Recommendation 16: The regions are building up national cooperation with a view to Danish participation in international collaborations, including Danish participation in the European Reference Networks (ERN) and Orphanet.	2	1	2
Recommendation 17: The regions build regional networks that support coordination of the regions' work between Danish ERN members, including the application process for the hospitals and contribute to the regional dissemination of relevant information from the Danish Health Authority.	3	3	1
Recommendation 18: The Danish Health Authority supports the regions in the above and strengthens Danish participation in ERN during the construction phase by: a) clarifying that hospitals with highly specialised functions are recommended to be part of a ERN, if a relevant network exists b) supporting the incorporation of Danish hospitals into international collaborations by mediating contact and providing information, for example by holding an information meeting when the next application deadline is known c) participating in Nordic cooperation, including the Nordic Network on Rare Diseases and Nordic Cooperation on Highly Specialised Treatment and Clinical Trials, where, among other things, cooperation opportunities in relation to ERNs are discussed.	1	1	2
Theme 5: Education and skills			
Recommendation 19: The teaching effort is strengthened, primarily in the specialist medical training programmes, in relation to diagnosis and treatment in rare diseases, so that all specialties in their target descriptions indicate learning competencies with a focus on the specialist being able to see symptoms as a possible part of a larger complex rare disease, so that relevant patients can be referred for investigation in the centres for rare diseases.	3	3	1
Recommendation 20: Relevant medical scientific societies prepare a description of how an expert training/further training regarding rare diseases can be composed.	3	3	2
Recommendation 21: It is being investigated how diagnosis descriptions for rare diseases can be anchored and expanded in the Medical Handbook in the future.	3	1	1

Recommendation 22: The necessary competencies of other health personnel who deal with patients with rare diseases are strengthened.	2	2	2
Theme 6: Registration, documentation and knowledge			
Recommendation 23: The regions and the Centres for Rare Diseases jointly: a) consolidate and expand the RAREDIS (Nordic database for rare diseases) nationally so that all relevant patients are included and strengthen the ongoing registration of rare diagnoses in clinical genetic departments b) ensure uniformly comprehensive registration practices, for example, by using explicit codes that enable the identification of rare diseases c) map existing databases and registers and their potential use, for example, with a view to integration in RAREDIS in collaboration with the regions' clinical quality development programme) d) strengthen research that includes patient processes both inside and outside the hospital.	2	3	1
Theme 7: Availability of treatment			
Recommendation on access to and research in Orphan Medicinal Products (recommendations from 2014): ▪ That it is ensured that there is (continued) access to necessary Orphan Medicinal Products in Denmark, including that transparency is used in pricing and subsidy schemes. ▪ That there is general attention to the opportunities for research, development and initiatives in the field in Denmark, including recommending that the Danish Centre for Rare Diseases as well as other relevant hospital departments and research institutions participate and positively support research in Orphan Medicinal Products.	2	1	1
Recommendation for support for participation in tentative experimental treatment (recommendations from 2014): ▪ Preliminary experimental treatment should continue to be possible and carried out where appropriate. ▪ That Denmark follows and participates in European initiatives in the field, such as clinical studies and collaboration on health technology assessments.	2	2	1
Recommendation on the possibility of referral for research-related treatment abroad (recommendation from 2014): Attention should be paid to the possibility of referral for specialised research-related treatment abroad, when there is a relevant opportunity for this.	1	1	2
Theme 8: Implementation			
Recommendation 1: That the Danish Health Authority holds an annual status meeting with the parties involved for the next 3 years regarding to ensure implementation of the recommendations and continued dialogue in the area.	1	1	1

	Recommendation on the institutional involvement of patient associations (recommendations from 2014): ▪ Voluntary associations should be involved in the work regarding the patient group's special problems, for example, as a hearing party for new legislative proposals with relevance to the area, in relevant working groups and so on, set up by public bodies and should be equipped to handle this task. ▪ Patient associations can be involved with great advantage in gathering experience, satisfaction surveys, and so on. ▪ That you support the commitment and participation of the Patient Associations.	1	1	3
	Recommendation on the inclusion of EUROPLAN's proposals and recommendations (recommendation from 2014).	1	1	3
Governance and organisational structures	*See theme 8 recommendations.* *Recommendation 1*: Implementation: The recommendation to hold an annual status meeting with the Danish Health Authority and the parties involved from the 2018 status evaluation is assessed to have been implemented. Since 2018, the Danish Health Authority has held an annual status meeting in 2019, 2020 and 2022, where in 2021 it was not possible to hold a status meeting due to the coronavirus 2019 (COVID-19) epidemic. In addition to the follow-up group, the Danish Health Authority has regularly invited actors who deal with rare diseases to the status meetings. The status meetings are based on the recommendations from the Danish Health Authority's status evaluation from 2018 (Følgegruppen, 2022), with which the members of the follow-up group discuss the status of the implementation of the recommendations and other relevant issues in the field. Through the interviews, it has come to the fore that there is satisfaction with the mechanism surrounding the meetings and the status being taken. However, two conditions are highlighted as having negative significance. On the part of the Danish Health Authority, there has been a replacement among the representatives, which, among other things, has limited continuity and knowledge transfer. In part, there has been strong representation from the regional health service, which is estimated to have resulted in limited attention to the local health service at the meetings. Impact: The interviews show that holding the annual status meetings has an effect in terms of implementing the strategy's recommendations. The professional dialogue and regular meeting cadence are considered to help maintain the prioritisation of the area among the various actors, and thus support the implementation of the recommendations. It is also emphasised that, during the situation with the COVID-19 epidemic, it has contributed to the fact that focus has largely been maintained despite the difficult conditions for work in the healthcare system. The status meetings are considered to be an important tool in the implementation of the recommendations. The meetings create space for professional discussions of current development trends, issues and challenges in the field, and contribute perspectives on how the work with the recommendations develops in practice. Finally, it is ensured that the area is continually adapted to national as well as international changes. Relevance: The recommendation to hold annual status meetings is still considered relevant as a mechanism for future work in the area. The interviews show that the status meetings are an important part of the strategy, as they help to ensure the implementation of the recommendations and contribute to prioritising and maintaining the activity in the area. The analysis also shows that in the further work it is essential to ensure the continuity of staffing and sufficient representation from relevant parties. Follow-up group members: ▪ Centre for Rare Diseases Aarhus University Hospital and Central Region			

	▪ Centre for Rare National Hospitals and the Capital Region ▪ Danish Society for Medical Genetics ▪ The National Association of Municipalities ▪ The Medical Handbook ▪ Region North Jutland ▪ Region South ▪ Sjældne Diagnoser (Rare Diagnoses - an umbrella association of 55 associations for citizens affected by rare diseases and disabilities) ▪ The National Board of Social Affairs and Health.
Funding model	*Overall funding model not mentioned. Comments related to sources of funding extracted.* *Areas for future focus – Need for clarity around finances in order to maintain competencies:* From the analysis, it can be deduced that several of the efforts initiated in connection with the status evaluation in 2018 are based on temporary funding. For a development purpose this is relevant, but the complexity of the area challenges this approach. The particular challenge with temporary funding in this area is that it has been difficult to maintain competencies. This is crucial, as the complexity of the field means that building skills takes extra time. Loss of knowledge at the end of a project is thus more difficult to handle here than in other areas. *In relation to Recommendation 6 (a):* In a future perspective, in relation to Centre for Rare Diseases at Rigshospitalet (CSS-RH)…Work is underway to establish a Centre for Rare Diseases for adults, which is expected to contribute to achieving this objective. As described, the conditions surrounding adults at Centre for Rare Diseases at Aarhus University Hospital (CSS-AUH) are unclear after the end of the project funding in mid-2022. *In relation to Recommendation 13:* In 2020, Sjældne Diagnoser, in collaboration with the Committee for Health Information, prepared a proposal for a project for virtual rare patient education inspired by the "Learn to tackle" model (Sjældne Diagnoser, 2020)…The background for the initiative was funds allocated with the Ministry of Health's empowerment grant 2018/2019-2021 for Rare Diagnoses, which are earmarked for patient education. However, the project description was never assessed, which resulted in unused funds from the empowerment grant in the Health Pool from 2018-2021. These were instead partially channelled into funding Helpline 2021/2022 (Følgegruppen, 2022). The immediate experience is that "Learn to tackle" cannot be used directly as a starting point, and there is a need for greater processing before existing models can be used in the rare area. This means that there is not yet a regular offer for people with rare diseases based on existing models. *In relation to Recommendation 15:* Helpline has so far been financed by a temporary grant, but is not financially secure for the future. If the consultancy is to continue, funds must therefore be added. Rældne Diagnoser estimates that additional funding is needed from and including the 4th quarter of 2023 and up to and including 2025 in order to keep the offer alive (Følgegruppen, 2022). *In relation to Recommendation 19:* Based on the evaluation, a need can thus be identified for a competence development effort as well as funds for this… *In relation to Theme 5 overall:* …there are good experiences with the applicability of the Medical Handbook rare articles, which is why it is crucial to find continued funding for this.

References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	*See recommendation 5.* However, it is debatable whether the full potential of the technological leaps is being reaped at this time. Among other things, it is emphasised in the interviews that there is less screening in Denmark than in other countries. The interviews also emphasize that the methods used today have been the same for a long time. Exome sequencing is often highlighted as new, but has in reality been carried out since 2013. However, even though it is now carried out as genome sequencing, the new data is still interpreted based on an older knowledge and framework of understanding, as not enough time is put into carrying out the in-depth analyses. It is thus assessed that there is still unfulfilled potential in this area.
Personalised medicine, genomics, genetic counselling	*See recommendations 4 and 5, and theme 7 recommendations on experimental treatments.* *Recommendation 5*: A central actor in the implementation of this recommendation is the National Genome Centre, which was established by law in 2018, and which has worked with better investigation and to develop and run Denmark's national infrastructure for personalized medicine. The potential here is great, which is why special attention is paid to ensuring clear priorities regarding who receives, for example, whole genome sequencing (Følgegruppen, 2022c). The establishment of the National Genome Centre has been a difficult process, which has drawn on resources among geneticists in the field. It is thus only at the time of the current evaluation (3rd quarter 2022) that the first sequencings have been carried out in this way. Hopes for the significance for both investigation and the preparation of personalised medicine are high. It is also relevant that the National Genome Centre has a special focus on rare diseases. But due to the strain on resources in the establishment phase, a number of patients have been waiting for their investigations, which is why there is now a sense of relief that the centre has really started. Although it is emphasised as essential to gather knowledge and resources, with the establishment of the centre certain ways are also chosen in which the analyses are carried out, which can limit some of the investigations. *Theme 7:* The evaluation shows that the opportunity for patients to participate in experimental treatment is limited in practice. On the other hand, the relevance of the recommendation to ensure the possibility of treatment abroad has changed, as systems for this have largely been established, just as with the establishment of European Reference Networks, work is being done in the direction of letting the expertise via knowledge sharing come closer to the patient.
Models of care/care pathways	*See recommendations 2, 3, 4, 6 and 8.* Efforts for people with rare diseases affect many different players in the healthcare system. Centres have been established in CSS-RH and CSS-AUH, who in their practice have close collaborations with a number of specialties, in particular the clinical genetic specialty and paediatrics. As investigation and treatment draw on a wide range of expertise, there is also collaboration in various ways with the other specialties, cf. the specialty plan, as well as with departments that carry out treatment at the main functional level. There is also collaboration with general practitioners and often close collaboration with the municipal efforts, which offer efforts depending on needs in the areas of children, family, health, employment, disability and care. The intention is that, in relation to the treatment at the hospitals, the centres act as a 'collection mechanism' for those patients who do not naturally fall under other specialties, see also the specialty plan. However, this has proven difficult in practice, as it requires the knowledge of each individual doctor for detection and action. This is challenged by the fact that, as a general rule, patients are not treated locally. This is further complicated by the fact that referral guidelines have not been drawn up as recommended. There is thus an unfulfilled potential here. A particular focus in the strategy from 2018 is to

	ensure better transitions for people with rare diseases from child to adult. It is thus also a transition from a collaboration between the centres for rare diseases and paediatrics to a possible collaboration between the centres and a large number of organ-specific 'adult specialities', where the patient will often belong to several. There have been initiatives at both centres to address this problem, but this still appears to be a very difficult task. Furthermore, extensive development has taken place within clinical genetics. In further work, there may be a focus on realising the potential of the improved methods, including working with a systematic focus on investigating patients without a definitive diagnosis. Likewise, this development creates other opportunities to capture and ensure the start of good patient processes.
Workforce	*See recommendations 7, 19, 20, 21 and 22.* The evaluation shows that the effort to ensure training and competences in the area overall has a very low degree of implementation. Part of the explanation for this may lie in the fact that there have been difficult conditions for skills development during the COVID-19 epidemic. Knowledge of rare diseases is thus not currently included in the revision of the specialist medical training, a description of what an expert training might look like has not been prepared, just as the further training efforts for "other health personnel" have taken place without an identified overall system for this. The low degree of implementation contrasts with the importance and relevance of meeting specialist staff, from specialist doctors to dietitians, therapists and the municipality's social and healthcare staff, who are prepared for the task. Thus, it is considered relevant that, in the further work, a clear plan is laid for upskilling in this area, which can be based both on practical learning and more traditional education. On the other hand, there are good experiences with the applicability of the Medical Handbook articles on rare diseases. However, no further funding has yet been found for this work.
European Reference Networks	*See recommendations 16, 17 and 18.* International cooperation has changed since 2014. The first recommendations contained a number of different elements, but since 2018 the focus has been mainly on establishing and participating in the ERNs. European Reference Networks comprise of 24 networks which, among other things, works with different groups of rare diseases in order to exchange knowledge and experience across European Union health services and health personnel. Denmark is now represented as a full member in 22 out of 24 networks and as Affiliated Partners in two ERNs (ERN Cranio and Ern EpiCARE), which is based on extensive efforts in this regard. Among the regions, there is a recognition of the opportunities and potential of international cooperation and the importance of benefiting from and benefiting from international competences when initiatives for people with rare diseases are discussed and organised. The document analysis shows that few regions have established networks that internally support the regions' participation in the ERN (Følgegruppen 2022). However, the interviews do not show examples of regional networks being built to support coordination of the regions' work between Danish ERN members. At the same time, there are only limited examples from the interviews of how collaboration in the ERN has concretely fertilised the specialist's other work with rare diseases. There is thus still unfulfilled potential here. Written statuses from the follow-up group and the interviews further illustrate that the regions' participation in international cooperation can appear as a competition between the regions (Følgegruppen, 2022f). There is therefore a desire for the regions to recognize and support each other to a greater extent in the various memberships, and share relevant knowledge.
EU alignment and participation	*See recommendations 16, 17 and 18, and theme 8 recommendation on the inclusion of EUROPLAN's proposals and recommendations.* A focus on expanding and continuing to ensure Danish participation in international networks is assessed in the evaluation to be able to strengthen efforts for people with rare diseases in Denmark, including the organisation of systematic knowledge sharing internally and across regions.

	Orphanet is an international network that works to collect knowledge about investigation, diagnostics and treatment of patients with rare diseases, has not yet been fully achieved. The regions use the Orphanet code system…but are not members of the network. In this connection, CSS-RH recommends that participation in the Orphanet collaboration be anchored in the centres, although this requires resources (Følgegruppen, 2022b). In addition, there is Danish participation in Nordic cooperation, for example, in Danish representation in the Nordic Network on Rare Diseases. In addition, the Danish Health Authority has managed in the build-up phase to encourage and support the regions' participation in international collaborations. Going forward, consideration can be given to how participation can continue to be supported and how experiences around participation can best be disseminated.
Health information (including rare disease registries)	*See recommendations 10 and 23.* The work to carry out a systematic and uniform registration is underway, but it is also an area where extensive development has taken place at the same time. Thus, a number of decisions about the direction and need for data are now pending, so that a basis can be formed for an agreement and thus a uniform registration practice in relation to the possibilities offered by the international collaborations and coding systems as well as the electronic patient records. However, this is also an area where special attention can be paid to the connection between yield and resource consumption.
Orphan medicines	*See theme 7 recommendations.* The analysis has shown that although the status evaluation from 2018 does not explicitly include the three themes from the strategy in 2014 on the development of medicine, participation in experimental treatment and access to research treatment abroad, there has been extensive development in the area. With the placement of assessments of new medicines in the Medicines Council, a system has been drawn up and expertise gathered, also with the inclusion of the special conditions for rare diseases. The assessment process is an area characterised by a number of dilemmas, for example, relative to uncertainty in assessments on a fragile data base mixed with high costs for new medicines for small patient groups.
Rare disease research	*See recommendation 23 and theme 7 recommendations.* …the analysis shows that within research in the area from 2014 to 2018 there has been a significant reduction in the focus of the recommendations. The analysis also shows that there are limited opportunities to prioritize resources for this. Without a strategic focus going forward on strengthening research, it is therefore assessed that it may prove difficult to develop the potential within this area.
Alignment beyond the healthcare sector	*See recommendations 8, 14 and 15.* *Recommendation 8 (Summary)*: Likewise, it may be useful to consider working with municipalities to provide them with a sufficient basis for implementing holistically oriented and coherent citizen courses. It is also noted that wording regarding the municipalities' efforts is less binding in the evaluation from 2018 than in the strategy from 2014. Efforts for people with rare diseases are often complex and draw on several different municipal efforts. This means that people with rare diseases and their families often meet several different municipal authorities and implementers, despite intentions to the contrary. In particular, challenges are experienced with the municipalities' efforts being granted on the basis of a functional ability assessment, and to a lesser extent involving knowledge of the disease behind it. For this group, this means that there are more experiences of the group being offered interventions that are not targeted at their needs. So there is potential in targeting efforts, including maintaining and developing structures for how relevant knowledge is secured for the municipalities, and how and when they seek this out.

	Recommendation 8: This recommendation has two focus areas; partly that the municipalities must ensure holistically oriented and coherent citizen processes, partly that municipalities with experience must make their knowledge available to other municipalities. From the municipal side, it is described how they have tried to ensure consistency with the requirements in the legislation in the other disability area, including that the municipalities work holistically, assess the citizen's needs based on the importance that a reduced functional capacity has for daily life (see the Service Act; Proclamation of the Social Service Act, LBK no. 170 of 24/01/2022, of which §1 states: "The purpose of this Act is... 3) to meet needs resulting from reduced physical or mental functioning or special social problems".), and coordinates processes from here. The Service Act's needs assessment is based on a functional capacity assessment… The main elements are to describe functional capacity with a focus on body, activity and participation – as well as the health and contextual (personal and environmental) factors that affect functional capacity. Roughly speaking, this means that a diagnosis is only significant to the extent that its manifestation has an impact on how the citizen can function in his everyday life. Municipal knowledge gathering and thus decision making and action will thus not (unlike the hospital) be targeted at a diagnosis, but rather at the limitation and the opportunities for expression that the citizen experiences in everyday life. In the evaluation, we see examples where decisions and efforts have thus been targeted at functional limitations more known to the municipality, even though the reasons have been very different. In some cases, this has meant that the efforts have not been comprehensive, which could have been avoided with a little more thorough research into not only the specific manifestation of the disease, but also the diagnosis behind it. In practice, this has given citizens unnecessary breaks in the initiated efforts. A holistic effort for a citizen with a rare disease thus often requires a different focus than what is currently the practice for the application of the functional ability assessment, as per the Service Act. Another factor that makes municipal work difficult is the structure of the municipalities, which means that there are many actors involved around citizens with complex needs. A child with extensive functional impairment (and the family around the child) will, for example, in the area of authority meet both authority caseworkers with a focus on child specialist investigations, help at home, aids, the family and the parents' employment situation as well as educational-psychological assessment. In the performing area, the family can use different suppliers of help, staff from or day care centres and school offers, training offers and other efforts. The family will also be able to receive interventions in the family department as well as employment interventions. For adults with rare diseases, the municipal landscape is also complex. This organisational complexity is not only challenging for people with rare diseases, but for vulnerable people in general. In national politics, there has thus been a great desire to ensure greater coherence, for example, the agreement on the upcoming main law which on several fronts is reminiscent of the recommendations that are assessed here. Finally, it is also significant that the municipalities have experienced increasing expenditure pressure in the social area (see for example, KL and Regeringen, 2021), which in the interviews is assessed to have had an impact on which offers are made available. This may also have contributed to the fact that the wording regarding the involvement of specific professional groups…has become less binding. In this context, several patients experience a problem in applying for support, if the costs for this fall into a grey area between aids and treatment means, for example a bag for medical equipment.
Any additional information (for example, background to the strategy or strategy development)	The national strategy from 2014 contains approx. 100 recommendations. The strategy was accompanied by follow-up work from the parties involved and also an agreed status evaluation, which was published in 2018 with the title "National Strategy for Rare Diseases – Status evaluation and recommendations for future efforts". The purpose of this status evaluation was to take stock of the strategy for 2014 and set the direction for further work. Thus, the status evaluation from 2018 brings together the approx. 100 recommendations in 23 recommendations divided into six themes that intend to be more action-oriented and clearer in actor focus.

	In order to provide a renewed overview of the area in 2022, results and experience with recommendations from the national strategy from 2014 and the status evaluation from 2018 have been collected and disseminated in this evaluation. Since the scope of the evaluation is complex as described, four central, methodological choices have been made in the evaluation design. ▪ **First choice – to be able to capture the complexity of the area** In order to capture and ensure interpretation of the complexity, the evaluation is organized based on qualitative methods. This choice has been made to capture the necessary nuances that the organizational complexity around rare diseases contains, including experiences, experiences and variations in patient flow. This is difficult to capture with a more quantitative approach. Against this background, the analysis is based on a document analysis and a large number of interviews with selected specialists and professionals in the regional and municipal healthcare system, supporting actors and associations. ▪ **Second choice – to involve specialist knowledge** In order to ensure relevant perspectives, knowledge and experience in the field, the evaluation is based on knowledge from various actors who work in the field. For the same reason, it has been prioritized to involve the Danish Health Authority's follow-up group for rare diseases (hereafter the follow-up group) in framing and focusing the evaluation. In addition, the evaluation draws on a number of experts from the follow-up group and from their working relationships as informants. In order to gain broad perspectives, however, we have also gone wider in the knowledge that the expertise in the field is gathered in a few hands. ▪ **Third choice – to create an overview and relevance of evaluation themes** In order to ensure a thorough review, comparison and systematization of the recommendations, the evaluation has started with a preliminary analysis. The aim here was to compare the approximately 100 recommendations from the national strategy from 2014 with recommendations in the status evaluation from 2018 to ensure that the evaluation themes used are the relevant ones. Based on the preliminary analysis, it can be inferred that with the transition from 98 recommendations in 2014 to 23 recommendations in 2018, a number of up-to-date clarifications have taken place, which have made the work more manageable and application-oriented. In addition, the preliminary analysis states: ○ That there have been shifts in content that can be interpreted as actual changes in focus on, among other things, recommendations on the municipal efforts, on which health professional groups should be involved, and on the availability of treatment. ○ That two themes are not explicitly covered by the six themes that appear in the status evaluation from 2018. These two have been added in this evaluation: A theme on "Availability of treatment" covers recommendations regarding access to medicine for people with rare diseases, around the work with trial, experimental treatment and the possibility of referral to research treatment abroad. Another theme deals with "Implementation" and contains recommendations from both 2014 and 2018 to maintain focus in the work to implement the strategy. ○ That from the status evaluation's appendix overview in 2018 compared with actual formulations from the national strategy from 2014 omit nine recommendations and that there are linguistic ambiguities in the transition between the two strategies. In order to ensure the inclusion of these insights, the evaluation thus focuses on eight themes and a total of 28 recommendations, just as the previously omitted recommendations have been included to the greatest extent possible to avoid uncertainty in relation to the basis on which the evaluation is based. ▪ **Fourth choice – to ensure a systematic and rigorous approach to the assessments** In order for the evaluation to create a renewed overview of the area at the same time as capturing the complexity, it has been crucial to have a systematic and rigorous approach. All recommendations are thus assessed from three evaluation perspectives: ○ Implementation – the question of whether and, if applicable, how a given recommendation is implemented.

	○ Impact – the question of whether and, if applicable, what (expected) positive impacts the recommendation has had for people with a rare disease. ○ Relevance – the question of whether the recommendation remains the relevant way to handle the challenge in question. Based on the evaluation, a discussion and assessment of these perspectives is thus carried out for each of the 28 recommendations.

Key: COVID-19: coronavirus 2019; CSS-AUH: Centre for Rare Diseases at Aarhus University Hospital; CSS-RH: Centre for Rare Diseases at Rigshospitalet; ERN: European Reference Network; RAREDIS: Nordic database for rare diseases.

Note: The information in this table was extracted from a version of the original document translated to English using Google Translate.

Table B9. Data extracted for England (Action Plan 2022)

England	Strategy information
Author(s) **Title**	Department of Health and Social Care England Rare Diseases Action Plan 2022[27]
Timeline	2021-2022
Overall aim(s)	Delivering improvements in diagnosis, awareness, treatment and care, and creating lasting positive change for those living with rare diseases.
Themes and or priorities	**Priorities** Priority 1: helping patients get a final diagnosis faster Priority 2: increasing awareness among healthcare professionals Priority 3: better coordination of care Priority 4: improving access to specialist care, treatments and drugs **Underpinning themes** ▪ Patient voice ▪ National and international collaboration ▪ Pioneering research ▪ Digital, data and technology ▪ Wider policy alignment ▪ Health equity.
Targets (if specified) and measurement method(s) (where available)	Each action lists an owner (*lead*), desired outcomes (*outputs and outcomes*), and how we will measure and report on progress (*action-specific monitoring and evaluation*). *'Outcomes' listed below may be considered as targets. Measurement methods are outlined under 'Action-specific monitoring and evaluation'.* **Monitoring and evaluation** All of the individual actions within this action plan are underpinned by a logic model, setting out the problem the action addresses, a clear organisational owner for the action, the outputs and outcomes that will be delivered, and the metrics which will be used to measure progress and effect of each outcome. Our aim is to improve the lives of people living with rare diseases and, in consultation with the rare disease community, following the publication of this action plan, we will also develop high-level metrics to support assessment of progress against each of the framework's priorities. This is likely to include specifically designed surveys to create baseline data against which to measure change. In so doing we aim to find robust approaches to address the following questions: ▪ do rare disease patients experience more rapid diagnosis?

	▪ has awareness increased among healthcare professionals? ▪ is care better coordinated? ▪ is there improved access to care, treatment, and drugs? As well as being able to report on the progress of each action, we aim to be able to measure progress in what matters to people living with rare diseases – improvements to the quality of care that they receive.
Implementation action(s), lead(s) and key performance indicator(s)	**Action 1: Improving how decisions are made on new-born screening for rare diseases** *Lead*: DHSC *Outputs*: ▪ Having already completed stakeholder engagement, a new United Kingdom (UK) National Screening Committee (NSC) terms of reference and remit. ▪ UK NSC Bloodspot Task Group terms of reference. ▪ UK NSC Bloodspot Task Group products: (1) baseline comparison between UK and European Organisation for Rare Disease (EURORDIS) key principles for newborn screening (2) manuscript advising on the methodological principles for screening test accuracy study designs in rare disease settings, such as newborn blood spot conditions. Expected to be published on gov.uk and to be submitted to a peer review journal (3) paper on technical and procedural considerations for modelling exercises around newborn screening to bring consistency to UK NSC modelling exercises (4) paper on use of registries in the newborn screening evaluation process. *Outcomes*: ▪ UK NSC structures and processes enabled to more fully support the research and evaluation effort in newborn screening/rare diseases. ▪ UK NSC methodological guidance available to inform the research effort in newborn screening/rare diseases. *Action-specific monitoring and evaluation*: ▪ UK NSC terms of reference publicised in spring 2022. ▪ UK NSC bloodspot task group terms of reference publicised in spring 2022. ▪ First new UK NSC meeting held in summer 2022 with research subgroup established, formal horizon scanning process defined, access to modelling capacity considered. ▪ First UK NSC bloodspot task group meeting held in spring 2022 with outputs defined, timescales set and intention to publish outputs stated. *Framework priority*: 1 **Action 2: Whole genome sequencing to screen for genetic conditions in healthy newborns – designing an ethically approved research pilot** *Leads*: Genomics England and National Health Service (NHS) England/Improvement (NHSE/I) *Outputs*: ▪ Pilot ready to implement at a small number of NHS trusts. ▪ Results pathway mapped for return of findings to NHS clinicians and patients. ▪ Mapping of NHS Pathways in place to support babies with positive results. ▪ Co-designed principles have been developed to underpin the candidate list of conditions to be looked for in the analysis. ▪ Modelling using existing data to determine yield of different analysis approaches to genomic newborn screening is finalised/available. *Outcomes*:

	▪ Clinicians across all relevant medical specialties have been engaged. ▪ Detailed plans are in place to capture patient experience of genomic newborn screening. ▪ Evidence for commissioning decisions on future genomic screening has been defined. *Action-specific monitoring and evaluation*: ▪ Number of NHS pathways in place to support families with positive results. ▪ Number of engagement interactions completed related to pilot implementation and research planning. *Framework priority*: 1, 3 and 4. **Action 3: Continuously develop the National Genomic Test Directory – including rollout of whole genome sequencing (WGS) that will play an important role in diagnosis of rare diseases** *Leads*: NHSE/I *Outputs*: ▪ Phase 2 and 3 clinical indications for WGS will be launched in 2021 to 2022. ▪ An annual process for updating the Test Directory will have been implemented in Q4 2021 to 2022. *Outcomes:* ▪ Patients in the NHS in England will be able to access a world leading NHS Genomic Medicine Service (GMS), offering the full repertoire of genomic testing technologies from single gene testing to WGS. ▪ The NHS GMS will support equitable access to genomics across the NHS in England and provide standardised care across the population. ▪ The NHS GMS will continue to implement new technologies as the testing strategy develops. *Action-specific monitoring and evaluation*: ▪ Patient Level Contract Monitoring data will show the genomic testing strategy is being delivered across England, with increased activity as the range of conditions on the Test Directory is expanded, and developments in technology are introduced in the NHS GMS. ▪ All 7 NHS Genomic Laboratory Hubs (GLHs) will be delivering the testing set out in the updated Test Directory, with regional variations monitored on a quarterly basis through performance data submitted to NHSE/I. (A subset of these data may be made publicly available, if clinically appropriate and in adherence with laws and data protection standards). ▪ All 7 NHS GLHs will have met the exit criteria for live clinical testing of WGS. *Framework priority*: 1 and 4. **Action 4: Further develop the Genomics England clinical research interface – increase the number of diagnoses from genome data, and provide evidence to support the NHS Genomic Medicine Service in developing its diagnostic Test Directory** *Leads*: Genomics England *Outputs*: ▪ NHS Genomics Laboratory Hub able to report new diagnostic results when returned under Diagnostic Discovery process. ▪ Researchers and clinicians communicate about complex results. *Outcomes:* ▪ Patients receive diagnoses. ▪ Analysis pipeline gains new test control samples. ▪ Researchers and clinicians can collaborate on new discoveries. *Action-specific monitoring and evaluation*:

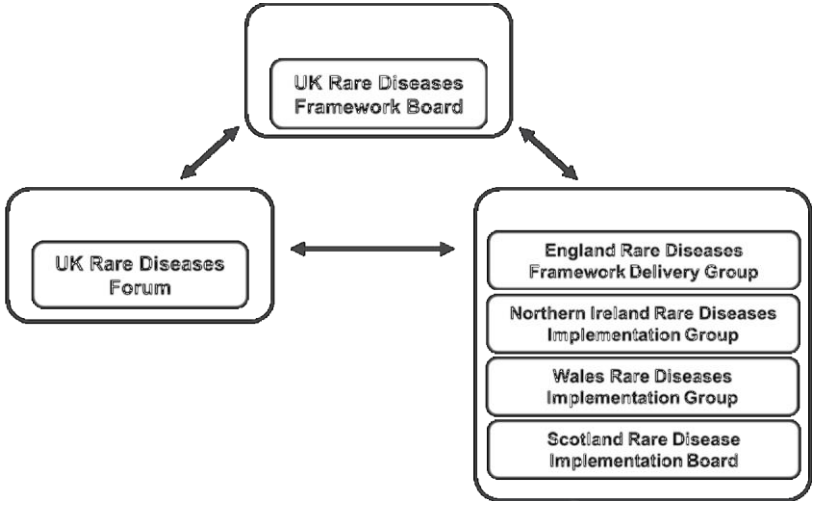
	▪ Number of potential diagnoses returned to the NHS; aiming to return >100 diagnoses per year, the exact number will be publicly reported. ▪ Number of papers published. *Framework priority*: 1 and 4. **Action 5: Pilot new approaches for patients with undiagnosed rare conditions** *Leads*: NHSE/I *Outputs*: ▪ Development of pilot approach(es) in April 2022. ▪ Selection of sites during summer 2022. *Outcomes:* ▪ An evaluated approach to testing new approaches to diagnosing individuals with rare diseases. ▪ Faster diagnosis and improved care for patients with undiagnosed conditions. ▪ Design and outcomes of the pilots and evaluations published, to help monitor impact and disseminate learnings. *Action-specific monitoring and evaluation*: Number of clinics piloted. *Framework priority*: 1 **Action 6: Develop an innovative digital educational resource ('GeNotes') – providing healthcare professionals with relevant and concise information to support patient management, linking to the NHS Genomic Test Directories, and signposting to extended learning opportunities** *Leads*: Health Education England *Outputs*: ▪ Phase 1: User testing and publication of a minimal viable product including resources for paediatricians, oncologists and general practitioners. Completed April 2022. ▪ Phase 2: Scale up content production for other specialities. April 2022 onwards with input/co-development with the rare disease community and Genomics Education Programme Public Patient Involvement (GEP PPI) group where appropriate. ▪ Phase 3: Evaluation of use and effectiveness of the resource. From October 2022. *Outcomes:* ▪ A central locale that brings together relevant clinical/scientific information and signposts to applicable guidelines and other supplementary clinical and scientific information. ▪ A more informed NHS workforce. ▪ An educational platform that can integrate with NHS and other digital systems via a functional Application Programming Interface (API), which allows two digital applications to talk to each other, thereby allowing NHS digital platforms to utilise content from GeNotes within their own system. *Action-specific monitoring and evaluation*: ▪ Impact evaluation will form phase 3 of this action. Full details are still to be determined, but are likely to include: - User experience (to include data from private and public beta phases) - Web analytics including API adoption, for instance how many NHS digital systems are 'talking with' and therefore using GeNotes content. - Impact metrics, for example self-evaluation by users on impact to practice. *Framework priority*: 2

	Action 7: Determine how best to include rare diseases in UK health professional education and training frameworks – to ensure rare disease competencies and learning outcomes are embedded in NHS education and training frameworks across all relevant specialities including general practice training and those involved with emergency care *Leads*: Health Education England *Outputs*: ▪ Review current UK health professional education and training frameworks (to include curricula, proficiency standards, etc.) to determine rare disease content. The review process will take place over the 2022 to 2023 financial year. ▪ Identification of rare disease competency needed for each education and training framework document, using existing generic curricula and competencies. Working with professional organisations, curriculum developers and other stakeholders (including patients/family members/carers identified through the GEP PPI group). ▪ Gap analysis to identify deficits in the inclusion of rare diseases in the frameworks. *Outcomes:* ▪ Awareness of which training programmes lack sufficient rare disease content. ▪ Increased amount of rare disease content included in education frameworks (will require additional actions in 2023 to 2024). *Action-specific monitoring and evaluation*: ▪ Percentage of education frameworks that include sufficient rare disease content. Change measured by repeating the review over time. *Framework priority*: 2 **Action 8: Extend the remit of the Genomics Education Programme to include non-genetic rare diseases** *Leads*: Health Education England (HEE) *Outputs*: ▪ Established links and agreed way of working or programme of work with key HEE programmes (for instance urgent and emergency care). ▪ Established and maintained links with integrated care systems (ICS). ▪ Rare disease education network to establish collaborations and share best practice. Membership of the network to include industry, third sector and research organisations, as well as other NHS organisations. ▪ Published rare disease hub webpage and resource library. *Outcomes:* ▪ Joined-up approach within HEE in regard to rare disease projects. ▪ Receive intelligence on workforce issues to inform workforce planning and new ways of working. ▪ Collaborative working and minimising duplication of effort. ▪ One-stop shop for clinicians to access rare disease education and training materials. *Action-specific monitoring and evaluation*: ▪ Establish links with fifty percent of relevant HEE programmes, for example Innovation and Transformation, Technology Enhanced Learning and agree joint programmes of work. ▪ Percentage of ICSs in England with established links created through regional HEE networks and HEE transformation leads. ▪ Number of members signed up to the rare disease education network. ▪ Web analytics of rare disease hub and resource library. *Framework priority*: 1 and 2.

	Action 9: Publish high-quality epidemiological and research papers to increase the understanding of rare diseases – including papers looking at basic rare disease epidemiology, impact of COVID-19 on people with some rare diseases and cancer-related risk factors or outcomes for people with some rare diseases *Leads*: NHS Digital *Outputs*: ▪ The National Congenital Anomaly and Rare Disease Registration Service (NCARDRS) will collaborate on and publish at least 6 papers describing novel findings or methods relevant to rare disease by the end of December 2022. ▪ NCARDRS will work with patient organisations to ensure visibility in their communities. ▪ Findings disseminated through presentations at conferences and other relevant events/platforms. *Outcomes:* ▪ Increased knowledge and raised profile of rare diseases through the publication of high-quality epidemiology and research. *Action-specific monitoring and evaluation*: ▪ Impact will be measured using Altmetric scores (a measure of the dissemination of a peer-reviewed paper via platforms like news outlets, social media, blogs). *Framework priority*: 2 **Action 10: Develop a toolkit for virtual consultations – improving use of videoconference and telephone clinic calls in services for patients with complex, multi-system rare diseases** *Leads*: NHSE/I *Outputs*: Toolkit published in spring 2022. *Outcomes:* ▪ Shared learning resources. ▪ Improved outcomes of virtual clinics for patients and families/carers. ▪ Sharing of issues that clinical teams need to consider in planning and delivery of virtual clinics. *Action-specific monitoring and evaluation*: ▪ Uptake of the toolkit within the Highly Specialised Portfolio will be monitored through annual clinical meetings. ▪ A survey will be developed for the services to determine whether patients and healthcare professionals found the toolkit helpful. *Framework priority*: 3 **Action 11: Support rapid access to drugs for patients with rare diseases in the NHS – assessing the complexity of the service in which the drugs will be used, by mapping available access initiatives, identifying drugs and delivery challenges through horizon scanning, and listing drugs that have been identified for access** *Leads*: NHSE/I *Outputs*: ▪ Map of programmes that promote access to drugs. ▪ Produce drug/service 'preparedness template'. ▪ Commissioning process developed to support rapid access to drugs. ▪ Report on whether or not there is access at the point of anticipated delivery, looking at: (a) if a drug is intended to be available on a certain date, is that the case, (b) is the uptake overall as expected and (c) is the geographical spread as expected.

	▪ Monitoring of access via Blueteq data. *Outcomes:* ▪ Rapid access to clinically effective and cost-effective drugs for patients with rare diseases. ▪ Improved understanding by the system of requirements to enable rapid access to take place. *Action-specific monitoring and evaluation*: ▪ High percentage of drugs available at anticipated date of delivery. ▪ Access initiatives mapped and narrative on progress provided. ▪ Commissioning processes to support rapid access to drugs developed. ▪ Ongoing list of relevant drugs developed and maintained. ▪ Measurement taken of whether or not there is access at the point of anticipated delivery and why there may be deviation from this. ▪ Findings summarised in England Rare Diseases Framework Delivery Group minutes/2023 action plan. *Framework priority*: 4 **Action 12: Develop a strategic approach for gene therapies and other advanced therapy medicinal products (ATMPs) – based on horizon scanning by NHSE/I** *Leads*: NHSE/I *Outputs*: An NHSE/I strategic approach for gene therapies. *Outcomes:* ▪ Clarity for the pharmaceutical industry, providers and patients around NHSE/I's strategic approach for gene therapies ▪ System prepared to deliver potential ATMPs if/when these are approved by the National Institute for Health and Care Excellence (NICE). *Action-specific monitoring and evaluation*: ▪ Development of a strategic approach by summer 2022, and narrative on progress provided. *Framework priority*: 4 **Action 13: Capitalise on the changes made to NICE's methods and processes to ensure that NICE continues to support the rapid adoption of effective new treatments for NHS patients with rare diseases – implementing NICE's new methods and processes to support access to new treatments for rare disease patients** *Leads*: NICE *Outputs*: ▪ Replace the end-of-life criteria with a severity modifier. ▪ Accept a greater degree of uncertainty when evidence generation is difficult, including rare diseases. ▪ Adopting process changes to help improve participation of patients and clinical experts, introducing a summary of information for patients as well as more flexibility to adapt consultation timelines for each appraisal to support more efficient timely access. ▪ Adopt refined highly specialised topic routing criteria. *Outcomes:* ▪ More therapies made available to rare disease patients more rapidly. ▪ Time efficient decisions made on topic routing. *Action-specific monitoring and evaluation*: ▪ Number of medicines for rare diseases receiving a positive NICE recommendation. *Framework priority*: 4

	Action 14: Monitor overall uptake of drugs for patients with rare diseases and map geographical access to those drugs *Leads*: NHSE/I and NHS Digital *Outputs*: ▪ Standard operating procedure for undertaking systematic component of variation (NHSE/I) ▪ Agree data flows, deliverables and cross-organisation resources to support exemplar equity of access project(s) based on population-based, patient-level data drawn from high-cost medicines data. *Outcomes:* ▪ Better understanding of the population uptake and impact of NHSE/I's high-cost drug commissioning policies and relevant NICE Technology Appraisals. *Action-specific monitoring and evaluation*: ▪ Annual report on update of drugs, including overall uptake and geographical equity using standard coefficient of variation. ▪ Plan of action agreed with any services where inequitable access identified. ▪ Evidence that this knowledge has informed future commissioning policy wording / NICE guidance ▪ Findings summarised in England Rare Diseases Framework Delivery Group minutes/ 2023 action plan. *Framework priority*: 4 **Action 15: Map the rare disease research landscape to identify gaps and priorities for future funding** *Leads*: Department of Health and Social Care (DHSC) and Medical Research Council (MRC) *Outputs*: ▪ Publicly available paper describing the rare disease research landscape, gaps, priorities, and levers for change *Outcomes:* ▪ Improved understanding of the rare disease research landscape. Better understanding of gaps, priorities, and levers for change. ▪ A better joined-up rare disease research community. ▪ Identification of opportunities for improved rare disease research addressing the priorities of the UK Rare Diseases Framework. *Action-specific monitoring and evaluation*: ▪ Project plan fully defined by spring 2022. ▪ Rare disease funding landscape mapped using existing databases by autumn 2022. ▪ Workshops held on gaps and priorities by end 2022. ▪ Paper published early 2023. *Framework priority*: 1, 2, 3, and 4. **Action 16: Reduce Health Inequalities in NHS highly specialised services (HSS) – including considering health inequalities at HSS annual clinical meetings, in service development and commissioning decisions, and in provider selection processes** *Leads*: NHSE/I *Outputs*: ▪ Discussion of health inequalities with all services April 2022 to March 2023. ▪ Repeat of geographic access exercise – September 2023. ▪ Explore how consideration of health inequalities can be incorporated into future HSS procurements – September 2023. *Outcomes:*

	▪ Increased understanding of health inequalities in highly specialised services resulting in more equal access and improvements for rare disease patients. *Action-specific monitoring and evaluation*: ▪ Discussion about health inequalities at all HSS clinical meetings. ▪ Paper about the outcomes of geographical access exercise to the NHS Rare Diseases Advisory Group. ▪ A log of how health inequalities have been considered in procurements. ▪ Log of which Highly Specialised Commissioning Team have undertaken training. ▪ Appropriate metrics before and after the intervention will be recorded for each service. ▪ Findings summarised in England Rare Diseases Framework Delivery Group minutes/2023 action plan. *Framework priority*: 4
Governance and organisational structures	**UK-wide implementation** To further help with implementation of the framework, two UK-wide boards have been created: the UK Rare Diseases Framework Board, providing high level coordination of rare disease policy and action plans across the 4 UK nations; and the UK Rare Diseases Forum, providing a way to engage a wide range of stakeholders in the rare disease community for advice and input (see Figure 1). The forum has two parts: a core membership which meets twice a year, and an online knowledge and collaboration platform for continual engagement with a broad range of stakeholders, which both feed into the strategic UK Rare Diseases Framework Board.  **Figure 1.** Governance structures for implementing the UK Rare Diseases Framework. Delivery or implementation groups are responsible for developing nation-specific action plans. The UK-wide UK Rare Diseases Framework Board provides strategic oversight and facilitates alignment of policy across the 4 UK nations. The UK Rare Diseases Forum, also UK-wide, provides a means of engagement with the community.

	England action plan The England Rare Diseases Framework Delivery Group develops, oversees, and coordinates delivery of England's action plans. It has brought together publicly-funded delivery partners across the health system including NHSE/I; NICE; the Medicines and Healthcare products Regulatory Agency; HEE; the NCARDRS; NHS Digital; Genomics England; the National Institute for Health Research (NIHR) and MRC, as major funders of rare diseases research; and representatives of rare disease patient and public voice and the clinician community. Over the course of 2021, the delivery group has met every 6 weeks to develop and agree on actions which have formed the basis of the plan. Following publication of this action plan, the delivery group will continue to meet to coordinate and report on delivery and develop actions for our second action plan in 2023. As well as the publicly funded delivery partners (listed in Annex B), whose actions are described here, there are also many other organisations with crucial roles in supporting people living with rare diseases and bringing about much needed change. These organisations include charities, patient advocacy groups, philanthropically funded organisations, independent policy institutes and industry. This action plan sits within this wider system and will help to facilitate continued engagement, increased co-ordination and more joined up working with others. **Monitoring and evaluation** Following publication of this action plan, the delivery partners which make up the England Rare Diseases Framework Delivery Group will continue to meet regularly to report on progress on these actions and identify any barriers to implementation which need to be resolved. We will also continue to work together across the 4 nations of the UK to align policy and share, and learn from, best practice. A central objective of this action plan is to improve transparency and to make sure that progress is visible to the rare disease community. The second England Rare Diseases Action Plan will be published at the start of 2023, and will report on progress against the actions set out here as well as proposing updated and new actions. **Future directions** During the coming year, the England Rare Diseases Framework Delivery Group will monitor and report on progress against the current actions. Progress will be reported in meeting minutes with a more detailed report in the second England Rare Diseases Action Plan at the start of 2023. At the same time, we will continue to engage with stakeholders through the UK Rare Diseases Forum and on-line platform to gather feedback on implementation of actions. As described above we will work with the rare disease community to develop an approach for monitoring and evaluation. We are aware that the rare diseases community has raised concerns which have not been addressed, or only partially addressed, in this action plan, which we will need to turn our attention to over the coming year. The England Rare Diseases Framework Delivery Group will continue to meet every 8 weeks and, as well as reporting on progress, will develop new actions to address outstanding community concerns. These will be informed by delivery partners' own engagement activities, feedback from the UK Rare Diseases Forum and on-line platform and workshops (such as those described above on NCARDRS and clinical research delivery).
Funding model	Funding for all the actions listed…is already committed, either through delivery partners' existing organisational budgets, or accounted for in the 2021 autumn budget and spending review. In this budget, the Chancellor announced a £5 billion investment over the next three years to increase health-related research and development. This includes funding to support Genomics England's research initiative, a national research pilot testing 100,000 newborns using whole genome sequencing to detect rare diseases with a genetic cause. **Progress to date** An additional £340 million of funding has also been announced, for the Innovative Medicines Fund, which will provide early access to promising new medicines, including cutting-edge gene therapies.

	(See 'Rare disease research' section below for information related to research funding)
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	*See Actions 1 and 2.* **Action 2: whole genome sequencing to screen for genetic conditions in healthy newborns** The UK NSC advises Ministers and the NHS in all 4 UK countries on all aspects of screening. Using research evidence, pilot programmes, and economic evaluation, the Committee assesses the evidence for national screening programmes against a set of internationally recognised criteria, taking a range of different factors into account. Proposals to screen for new conditions are considered in an annual call for topics which runs between September and December each year. Currently 9 rare conditions are screened for in newborns through the NHS Newborn Blood Spot Screening Programme. As part of England's Rare Diseases Action Plan, the Department of Health and Social Care commits to improving how decisions are made across the UK on newborn screening for rare diseases. In the year ahead this will be actioned through: ▪ a new UK NSC with a broader remit, revised terms of reference, and greater collaboration with researchers and stakeholders, including those with an interest in rare disease ▪ establishing a UK NSC Bloodspot Task Group to identify practical and innovative approaches to facilitate research and evidence which will inform evaluations of blood spot screening Opportunities will also be taken to engage internationally and learn from, and contribute to, international best practice on screening. Work is underway to produce a paper which compares the UK NSC bloodspot screening policy processes and programme delivery to proposed EURORDIS newborn screening criteria for good practice, to identify any areas of good practice and areas for improvement. This will provide an understanding of how UK screening policy and practice compares with an important, patient-defined, checklist. Further details of UK NSC's international activities are provided in the National and international collaboration section. The new UK NSC is set to commence work in summer 2022. **National and international collaboration** International collaboration is also vital for screening policy. The UK National Screening Committee (NSC) has links with policy making bodies in many countries. Further to this, the NSC's discussion about newborn screening for the rare condition severe combined immunodeficiency (SCID) was informed by contact with New Zealand, the US, and the Netherlands, the learning of which is being transferred and used to inform the evaluation of SCID screening in the UK. UK screening programmes are linked to European networks to further facilitate improved international engagement. The programme's laboratory adviser is currently President of the International Society of Neonatal Screening. This has facilitated links with German contacts in the discussion about whole genome sequencing in the newborn screening programme. The UK NSC will also continue to work with Genomics England on whole genome sequencing and this will bring opportunities to broaden international relationships with initiatives such as Screen4Care. **Health equity** Certain rare conditions, such as sickle cell disease, SCID and tyrosinaemia, disproportionately affect minority ethnic groups or communities, and it is important that these are not overlooked. An in-service evaluation of newborn screening for SCID has begun and a consultation on

	newborn screening for tyrosinaemia by the UK NSC is currently underway. Barriers to entry for clinical trials, including the need for services to be delivered locally, will be considered as part of the workshop on clinical research delivery mentioned above.
Personalised medicine, genomics, genetic counselling	*See Actions 2, 3, 4, 6, and 8.*
Models of care/care pathways	*See Actions 5, 10, 11, and 16.* **Integrated care systems** Health and care needs for individuals with rare diseases are complex, requiring collaboration across both the health and care systems. To support more integrated care across the system, the government ICSs in 2018 – partnerships between the organisations that meet health and care needs across an area, to coordinate services and to plan in a way that improves population health and reduces inequalities between different groups. ICSs provide an opportunity to further align the design, development and provision of services – including specialised services – with linked care pathways, where it supports patient care, while maintaining consistent national standards and access policies across the board. Taking this further, the Health and Care Bill proposes to build on the work of existing non-statutory ICSs by putting integrated care boards (ICBs) on a statutory footing to replace clinical commissioning groups as local commissioners, and requiring the creation of integrated care partnerships in each local system area. This proposes to give ICBs clear responsibilities, empowering them to better join up health and care, improve population health and reduce health inequalities. Giving ICBs responsibility for commissioning as many of the services that are accessed by their population as possible is a key enabler for integrating care and improving population health. It gives the flexibility to join up key pathways of care, leading to better outcomes and experiences for patients, and less bureaucracy and duplication for clinicians and other staff. Currently NHSE/I commissions all specialised services (the 149 'prescribed' services as set out in regulations). The Health and Care Bill includes powers which, if passed, will enable NHSE/I to delegate its functions to other NHS bodies, individually or jointly. NHSE/I is considering how it can use new powers in respect of delegating commissioning responsibility for some specialised services to ICBs individually and jointly. This would be with a view to realising the benefits of more integrated pathways, joined up care and population health management approach for specialised services and their patients where appropriate. For all specialised services, NHSE/I will remain accountable for their commissioning, and so continue to set consistent national service standards, and evidence-based access policies, which should be consistently applied across the country. For those services for which commissioning responsibility is delegated, NHSE/I will carry out assurance of the commissioning activity. Highly specialised services are characterised by small numbers of patients being treated by a small number of providers, using complex treatments. Therefore, delegating commissioning responsibility to ICBs is unlikely to be the appropriate route to realising the benefits of more integrated care. This will better be achieved through involving ICBs in the design of pathways and the development of pathways, and working with local systems to deliver care in a more joined up way. Primary and secondary healthcare providers will need to work with specialist centres to join up pathways and provide integrated interfaces for patients. Development and implementation of sustainable, meaningful metrics to measure the impact of these changes on rare disease care will require collaboration across delivery partners, including NHSE/I and NCARDRS, with input from rare disease stakeholders. These metrics should be used as part of assuring commissioning activity.
Workforce	*See Actions 6, 7, and 8.*

European Reference Networks	**National and international collaboration** Although the UK is no longer able to participate as a member of the European Reference Networks (ERNs), many UK clinicians and patient advocacy groups continue to collaborate effectively with ERNs across Europe. At a national level, NHSE/I has developed and implemented a process for recognising rare disease collaborative networks (RDCNs). RDCNs are made up of providers (rare disease collaborative centres) who have an interest in a particular rare disease and are committed to working together to progress research, increase knowledge and improve patient experience and outcomes. There are currently thirteen RDCNs in place (listed in Annex E). While the networks are coordinated by NHSE/I, providers can be from across the UK, and NHSE/I welcomes both national and international collaboration with RDCNs, including with ERNs to ensure the best standards of care for patients. NCARDRS is currently working with the RDCN for Congenital Thoracic Malformations to explore how disease registration can be utilised to support the delivery of national UK-wide clinical care for rare conditions by these emerging networks.
EU alignment and participation	**National and international collaboration** We will also continue to build upon and explore new opportunities for international collaboration including through the current European Joint Programme for Rare Disease (EJP RD); and the proposed European Partnership on Rare Disease (which is expected to succeed the EJP RD). It will be important to assess what assets and programmes of relevance to rare disease research, the UK might use to contribute to the goals of this new Partnership, while also investigating the possibility of leading new research actions. We will engage in policy developments emerging from the recent United Nations Resolution 'addressing the challenges of persons living with a rare disease and their families'. As set out in the National Disease Registration Service Direction we will ensure the UK can continue to contribute to Orphanet (so that UK data is included in the database) while also making use of this unique global information portal and its nomenclature for coding Rare Disease. We will also look to further align with international stakeholder engagement exercises such as the Rare 2030 foresight study, which gathered the input of a large group of patients, practitioners and key opinion leaders to propose policy recommendations, under the leadership of EURORDIS-Rare Disease Europe. The World Health Organization (WHO) is currently designing the establishment of a Global Network for Rare Diseases (GNRD). This network will pool resources and connect centres of excellence around the world, to improve diagnosis and care for people living with a rare disease. Over the next year we will engage with WHO to support their work on setting up GNRD, and determine how centres of excellence in England could best engage with and support this network.
Health information (including rare disease registries)	*See Actions 6, 9, 14, and 16.* **National and international collaboration** We continue to work closely with our counterparts in the devolved administrations to ensure close alignment of the rare diseases action plans each of the 4 nations is developing. One important area of collaboration is on national registries for congenital anomalies and rare diseases. Registries already exist in England and Wales, with a registry under development in Scotland. Work is also underway in Northern Ireland towards developing a rare disease registry. All 4 nations of the UK have committed to working together to make sure that registry activities align so that we can begin to achieve truly national disease registration. This will mean that we will have some of the largest population-based rare disease cohorts in the world and allow us to compare activity and outcomes across nations. Over the next year the national registries will establish a formal work schedule to produce a plan for how to achieve standardisation of the minimum core dataset and inclusion criteria, coding and routine analysis, as well as prioritising efforts regarding development of new methods to support rare disease registration and output. This will also include taking into account stakeholder input on priorities and acceptable practice, meeting fair processing obligations, and including opt out systems for individuals.

	Monitoring and evaluation One way of measuring change is through NCARDRS, which has been directed by the Secretary of State for Health and Social Care to collect data "to help the NHS in England, researchers, charities, people with congenital anomalies and rare diseases, and the public understand the prevalence of congenital anomaly and rare disease in England and to support wider understanding and treatment of these conditions". We will utilise the expertise and infrastructure within NCARDRS (NHS Digital) to understand the impact of relevant actions using patient level data.
Orphan medicines	*Not mentioned explicitly, however, see Actions 11, 12, 13, and 14.*
Rare disease research	*See Actions 1, 2, 4, 9, 13, 14, and 15.* **Pioneering research** The UK has particular strengths in rare disease research. Alongside charities, industry, and other organisations, the government primarily funds research into rare diseases via the NIHR and UK Research and Innovation (UKRI). One prominent initiative is the rare diseases component of the NIHR BioResource, which works in over 50 disease areas to link genetic information to clinical characteristics in order to provide greater understanding of disease mechanisms for the development of new treatments and diagnostics. As of December 2021, NIHR BioResource has recruited over 21,230 patients with rare diseases from 50 NHS trusts in England. All participants are genetically characterised and have given consent to be recalled for clinical studies including trials for new treatments. Over the next five years we will provide £40 million of new funding to the NIHR BioResource. The NIHR has also invested £816 million to support the infrastructure of 20 Biomedical Research Centres (BRCs) around the country. BRCs enable effective collaboration between world-leading universities and NHS organisations, bringing together academics and clinicians to translate laboratory-based scientific breakthroughs into potential new treatments, diagnostics, and medical technologies. The centres undertake themed research across a range of disease and therapeutic areas, including rare diseases, genomics, stem cell therapy and regenerative medicine. NIHR also supports the delivery of research funded by medical research charities and the life sciences industry through NIHR Clinical Research Facilities - purpose-built facilities in NHS hospitals where researchers can deliver early-phase and complex studies - and the NIHR Clinical Research Network which supports the set up and delivery of clinical research in the NHS and in other health and care settings. UKRI's MRC also has a strong focus on rare diseases. The MRC's Population and Systems Medicine Board supports the UK Rare Diseases Framework, encouraging the scientific community to come forward with their best ideas aimed at addressing research questions related to rare conditions. UKRI funds world-leading institutes such as the MRC Laboratory of Medical Biology, MRC London Institute of Medical Sciences, the Francis Crick Institute and Health Data Research UK. National leadership and capacity is provided by assets such as world-leading cohort studies (for example, UK Biobank and Born in Bradford) and MRC units and centres at the cutting-edge of human genetics, mitochondrial biology, metabolic diseases, and biostatistics. For businesses, the Innovate UK-supported Catapult network provides a gateway to supercharge innovation in the discovery and development of medicines, including cell and gene therapies. **Health equity** To ensure that the benefits of genomic healthcare are relevant to all communities, Genomics England is working on a 'Diverse Data' initiative to increase representation of minority groups in genomic research programmes. The initiative aims to tackle health inequalities by recruiting at least 15% of people from ethnic minority backgrounds to take part in research programmes, thereby reducing the historical bias towards populations of European ancestry.

Alignment beyond the healthcare sector	**A holistic approach to care and support** Despite ongoing advances in medical science, the vast majority of rare diseases currently have no effective, disease-modifying treatment. It is therefore also important that individuals and families living with rare conditions have access to timely advice, aids and equipment, and support in managing both symptoms and the wider impact of the disease. Improving coordination of care for rare diseases goes beyond treatment, requiring holistic consideration of the support needs of individuals and families across a wide range of public services. Over the course of the coming year, we will look at ways in which the provision of advice for rare disease patients can be improved, including clearer signposting to existing sources of support, and how we can coordinate with other government departments to ensure an integrated package of care. Recognising that many people living with rare diseases face additional physical challenges, we will also seek to align with other policy areas which address the complex needs of people living with rare diseases (such as the National Disability Strategy), further details of which can be found in the Wider policy alignment section. **Mental healthcare and rare diseases** We recognise that people living with rare diseases and their families often have very specific needs for mental health support and that this needs to be well coordinated with their wider health and social care. We are committed to exploring this further in future action plans.
Any additional information (for example, background to the strategy or strategy development)	**Community engagement** In developing the UK Rare Disease Framework, and now this action plan, we have placed the needs of those living with rare diseases at the forefront. With the support of Genetic Alliance UK, we recruited representatives of patient and public voice to both the England Rare Diseases Framework Delivery Group and UK Rare Diseases Framework Board. We have used the UK Rare Diseases Forum online platform to engage continuously with a broad range of people from the rare diseases community, providing an opportunity for discussion and feedback, as well as a source of updates on progress and related initiatives. We have also held two community roundtables to seek input on the draft actions and action plan, again with participants recruited with support from Genetic Alliance UK. In November 2021 we launched a targeted online questionnaire to gather detailed feedback on draft actions from people and organisations across the rare disease community. The questionnaire was open for three weeks and received 92 responses from people living with a rare disease, their carers, and family members, rare disease charities, healthcare professionals, industry partners and researchers. We also held a workshop in partnership with Breaking Down Barriers (a network of over 50 organisations working together to improve the lives of families from diverse and marginalised communities) to better understand health inequalities experienced by people from diverse and marginalised communities affected by rare conditions. Our delivery partners have also proactively engaged and sought extensive feedback from the rare diseases community as they have developed their actions. For example, NHSE/I hosted engagement sessions with more than 80 individuals representing over 50 different organisations, including patient charities, patient advocacy groups, medical royal colleges, and academics. Further details of engagement activities can be found in Annex C. **Current context** Progress in developing this action plan has taken place against the backdrop of the current COVID-19 pandemic, which has caused significant disruption to health and care services. The effects are ongoing, with the emergence of the Omicron variant and the need to support the vital increase in the vaccination programme having had a significant national impact on the NHS. The impact of the pandemic has been particularly severe on the rare disease community, as highlighted by the ARDEnt report, 'Making the Unseen Seen: Rare disease and the lessons learned from the COVID-19 pandemic', and a 2020 EURORDIS-Rare Disease Europe Rare Barometer Survey. A focus on COVID-19 has meant that some routine and primary care services have been scaled back, leading to delays or cancellations in diagnostic testing, transfusions, surgeries, scans, and routine appointments. Similarly, safety considerations, redeployed staff and travel restrictions

	have caused additional barriers to rare disease research, where cohort sizes are already small. Resources have also been diverted to much-needed COVID-19 initiatives, including the development of both vaccines and therapeutics against severe disease. This has affected the operations of many other services and, while we recognise these need to be built back up, this will take time. Plans are underway to put workforce and technology at the heart of long-term planning across the health service. It was recently announced that HEE, NHS Digital, NHSX and NHSE/I are to become one organisation. This will enable patients to benefit from the best care possible, thanks to a highly skilled workforce and faster digitalisation services. By transitioning these organisations into one, the government and the NHS are ensuring the health and social care sector is fully equipped to face the future and deliver for patients. While work will be needed to finalise logistics, the changes will ultimately better support the recovery of the NHS, address waiting list backlogs and support hardworking staff, all while driving forward an ambitious agenda of digital transformation and progress. Our commitment to improving the lives of those living with rare diseases remains as strong as ever, and we will look to learn lessons from the experiences from the COVID-19 pandemic. While ambitious, this action plan is therefore also realistic, recognising that it may take time to implement change within the current context. **Health equity** Some people living with rare diseases may face additional barriers to accessing services and support, beyond the immediate challenges of their condition. The principles of the framework commit the 4 nations to "ensure any impacts on health inequalities are considered when developing action plans". This includes involving a diverse range of voices at every level of policy development. As part of the development of England's action plan, we have sought to better understand the health inequalities experienced by people from diverse and marginalised communities who are affected by a rare condition, and to explore how health inequalities could be addressed under each of the framework priorities. The Breaking Down Barriers workshop and stakeholder publications such as the "Whose Voice is it Anyway?" meeting report (summarising the findings of an NHSE/I engagement session hosted by RareQoL and Medics 4 Rare Diseases) highlighted a number of common themes, including the need for: ▪ a holistic approach to care and support, which considers the needs of the whole family, both at the point of diagnosis and over the longer term ▪ accessible resources, taking into account people's lived experiences, and the challenges associated with communicating complex medical terms across cultural and language barriers ▪ developing and maintaining trust in healthcare professionals.

Key: API: Application Programming Interface; ATMPs: advanced therapy medicinal products; BRC: Biomedical Research Centres; COVID-19: coronavirus 2019; DHSC: Department of Health and Social Care; EJP RD: European Joint Programme for Rare Disease; ERN: European Reference Networks; EURORDIS: European Organisation for Rare Disease; GEP PPI: Genomics Education Programme Public Patient Involvement; GLH: Genomic Laboratory Hubs; GMS: Genomic Medicine Service; GNRD: Global Network for Rare Diseases; HEE: Health Education England; HSS: highly specialised services; ICB: integrated care boards; ICS: integrated care systems; MRC: Medical Research Council; NCARDRS: National Congenital Anomaly and Rare Disease Registration Service; NHS: National Health Service; NHSE/I: NHS England/Improvement; NICE: National Institute for Health and Care Excellence; NIHR: National Institute for Health Research; NSC: National Screening Committee; RDCN: rare disease collaborative networks; SCID: severe combined immunodeficiency; UK: United Kingdom; UKRI: UK Research and Innovation; WGS: whole genome sequencing; WHO: World Health Organisation.

Table B10. Data extracted for England (Action Plan 2023)

England	Strategy information
Author(s) **Title**	Department of Health and Social Care England Rare Diseases Action Plan 2023: Main report and annexes[28, 30]
Timeline	2023
Overall aim(s)	England's first action plan, published on 28 February 2022, included 16 specific, measurable actions under each of the framework's priorities. Based on extensive engagement with the rare disease community, it also set out key challenges, and identified focus areas for future work. This is England's second action plan, developed with delivery partners across the health system and in collaboration with people living with rare conditions. It contains a progress report on actions from the first action plan, and details of new actions for the year ahead.
Themes and or priorities	**Priorities** Priority 1: helping patients get a final diagnosis faster Priority 2: increasing awareness among healthcare professionals Priority 3: better coordination of care Priority 4: improving access to specialist care, treatments and drugs **Underpinning themes** ▪ Patient voice ▪ National and international collaboration ▪ Pioneering research ▪ Digital, data and technology ▪ Wider policy alignment **Focus areas** Recognising that not all concerns of people living with rare conditions could be addressed in England's 2022 action plan, we committed to considering how best to take forward outstanding areas of priority for the community. Informed by stakeholder engagement, we identified 6 focus areas for 2023 ▪ support for people with non-genetic and undiagnosed conditions ▪ coordination of care ▪ mental health and psychological support ▪ clinical research delivery ▪ registries ▪ monitoring and evaluation (development of high-level metrics).
Targets (if specified) and measurement method(s) (where available)	Key commitments in this action plan include: ▪ increasing data sharing between National Health Service (NHS) England, National Congenital Anomaly and Rare Disease Registration Service (NCARDRS) and Genomics England, benefitting patients by improving our understanding of equity of access to genomic testing and supporting interpretation of genomic test results

	▪ improving the way in which services for rare diseases are commissioned, through ensuring service specifications support coordinated access to specialist care, treatment, drugs, social care, mental health and special educational support ▪ improving the Be Part of Research platform, to make it easier for people living with rare diseases to participate in research, should they choose to do so ▪ addressing health inequalities for people living with rare diseases by gathering the evidence needed to include rare diseases in NHS England'sCore20PLUS5 framework, and enabling integrated care systems (ICSs) to develop targeted actions to reduce these inequalities(https://www.england.nhs.uk/about/equality/equality-hub/national-healthcareinequalities-improvement-programme/core20plus5/) ▪ evaluating the effectiveness of the United Kingdom (UK) Rare Diseases Framework and England's Action Plans in making a difference to people living with rare diseases *Note: Details of 2022 actions below include the owner (lead), progress report, action status, and metrics and milestones for 2023 (targets, measurement methods and KPIs). New actions for 2023 are listed with an owner, outputs, outcomes, and action-specific monitoring and evaluation (targets, measurement methods and KPIs).*
Implementation action(s), lead(s) and key performance indicator(s)	**<u>Annex A: progress against actions in England's 2022 Rare Diseases Action Plan</u>** ***Priority 1: helping patients get a final diagnosis faster*** **Action 1: improving how decisions are made on newborn screening for rare diseases** *Owner*: Department of Health and Social Care *Progress report*: ▪ the UK National Screening Committee (NSC) terms of reference and new remit was established in 2022 ▪ terms of reference established for the UK NSC Bloodspot Task Group in2022 ▪ draft manuscript on baseline comparison between UK and European Organisation for Rare Disease (EURORDIS) discussed at November 2022 meeting of Bloodspot Task Group ▪ report on the methodological principles for screening test accuracy is in progress ▪ commissioning briefs are in progress for research into technical and procedural considerations for modelling exercises, and use of registries. *Action 1 status (ongoing, extended or concluded)*: ongoing *Metrics and milestones for 2023*: ▪ the UK NSC will continue work to improve the evidence available to them in evidence reviews ▪ draft manuscript on baseline comparison between UK and EURORDIS completed by spring/summer 2023 ▪ draft report on methodological principles for screening test accuracy prepared for discussion with UK NSC and Netherlands Health Council in spring/summer 2023 ▪ commissioning briefs ready for procurement in 2023. **Action 2: whole genome sequencing (WGS) to screen for genetic conditions in healthy newborns – designing an ethically approved research study** *Owner*: Genomics England, NHSE *Progress report*:

	▪ research study due to begin during 2023 – all necessary systems, processes, education and training will be embedded before recruitment commences ▪ more than 150 clinicians have been engaged in preparation for mapping of results and healthcare pathways – this will be completed during 2023 ▪ four principles for gene selection have been finalised following an extensive engagement process, including an online survey that received over 400 responses. Assessment of genes against these principles is due to be completed in mid-2023 ▪ in 2022, data from 14,785 genomes from the National Genomic Research Library (NGRL) was used to model and test different approaches to the technical details or the analysis pipeline. Consultation on the outputs of this modelling with NHS and other genomics experts is currently underway. *Action 2 status (ongoing, extended or concluded)*: extended *Metrics and milestones for 2023*: ▪ optimal method for taking samples from newborns for the purposes of WGS ▪ data from the Baby and Mum Samples Study analysed and reported through Genomics England website (results anticipated in the first half of 2023) ▪ a list of genes and variants to be included in the screening panel, finalised and published over the next year ▪ participant information materials and website developed with approval by a Research Ethics Committee ▪ training for healthcare professionals involved in the study with training delivered at least 3 NHS sites ▪ Research Ethics Committee-approved research study rolled out in a small number of NHS trusts ▪ evaluation strategy developed with processes established to capture data that informs the value of the programme, including with respect to health economic outcomes. **Action 3: continuously develop the National Genomic Test Directory, including rollout of WGS, which will play an important role in diagnosis of rare diseases.** *Owner*: NHS England (NHSE) *Progress report*: ▪ the Test Directory is regularly updated to reflect scientific and technological developments, including new clinical indications for rare disease and WGS ▪ in October 2022, testing for the rare lung condition Pulmonary Alveolar Microlithiasis was added to the directory ▪ 31 rare conditions are now included within the eligibility criteria for WGS, meaning access for more patients. *Action 3 status (ongoing, extended or concluded)*: concluded *Metrics and milestones for 2023*: ▪ there will be future updates to the Test Directory. **Action 4: further develop the Genomics England clinical research interface – increase the number of diagnoses from genome data, and provide evidence to support the NHS Genomic Medicine Service in developing its diagnostic Test Directory** *Owner*: Genomics England *Progress report*: ▪ 1000 diagnoses have been returned to the NHS during 2022, against an original target of 100. *Action 4 status (ongoing, extended or concluded)*: concluded

	Metrics and milestones for 2023: ▪ the clinical research interface is now embedded within Genomics England and within the NHS Genomic Medicine Service. Diagnoses continue to be made and returned to the NHS on a monthly basis for participants of the NGRL ▪ it is anticipated that numbers will continue to go up year on year as the number of participants and researchers within the NGRL increases. **Action 5: pilot new approaches for patients with undiagnosed rare conditions** *Owner*: NHSE *Progress report*: ▪ the syndrome without a name (SWAN) pilot has been developed, aiming to reduce time to diagnosis for patients with undiagnosed rare diseases ▪ the proposed model covers all ages and aims to provide good geographical coverage. *Action 5 status (ongoing, extended or concluded)*: ongoing *Metrics and milestones for 2023*: ▪ the model is being discussed through NHSE governance and finance structures. If relevant funding is agreed, the SWAN pilot will be implemented in 2023. ***Priority 2: increasing awareness of rare diseases among healthcare professionals.*** **Action 6: develop an innovative digital educational resource (Genomic notes for clinicians (GeNotes)) – providing healthcare professionals with relevant and concise information to support patient management, linking to the NHS Genomic Test Directories, and signposting to extended learning opportunities** *Owner*: Health Education England (HEE) *Progress report*: ▪ private beta phase testing for oncology, paediatrics and general practice has been successfully completed ▪ GeNotes scored 91 out of 100 on the system usability scale assessment, with 93% of testers likely or very likely to use GeNotes in future ▪ the public beta platform for GeNotes was launched in June 2022 with oncology, and has achieved more than 36,800 page views and over 15,000users as at 30 January 2023 ▪ expansion of the Genomics Education Programme continues to support further and broader content created, and a Patient Advisory Group (Patient Advisors for Genomic Education – PAGE) has been established ▪ continued evaluation for the use and effectiveness of the resource is ongoing. *Action 6 status (ongoing, extended or concluded)*: extended *Metrics and milestones for 2023*: ▪ evaluation of resources will continue through 2023. Upcoming improvements include: ▪ advanced search and better filtering ▪ improved 'In the Clinic' specialty landing pages ▪ enhancements to Knowledge Hub ▪ next phase: pilot to syndicate GeNotes to primary care systems and exploring demand for a GeNotes app ▪ further specialities are planned to launch in spring/summer 2023, including: foetal and women's health, cardiology, primary care, pharmacogenomics, paediatrics and endocrinology

	▪ scale up content production for specialities from April 2023 onwards and resource being allocated to new specialities, for example neurology, nephrology and haemato-oncology. **Action 7: determine how best to include rare diseases in UK health professional education and training frameworks** *Owner*: HEE *Progress report:* ▪ since the publication of the 2022 Action Plan, HEE has adapted its approach to the development of healthcare competencies, resulting in a change to how it evaluates the impact and measures the inclusion of genomics and rare disease in healthcare workforce education and training ▪ HEE continues to work collaboratively with the Academy of Royal Colleges to evaluate medical curricula and ensure an increase in genomic and rare disease content. Whilst successful (particularly in paediatric, obstetric and oncology curricula), this has not been quantified and recorded as a percentage rise ▪ HEE's current (additional) approach to rare disease competency frameworks is 3-fold: o to develop role- or profession-specific frameworks through the introduction of the clinical pathway initiative o competency frameworks for the leaders of genomic medicine (genomic advisors) o nursing- and midwifery-specific competency frameworks. ▪ HEE is evaluating uptake, acceptability and efficacy using a case study method using quantitative scoring and qualitative thematic analysis ▪ through its clinical pathway initiative, HEE is identifying patient touchpoints, competencies required and education and training interventions, to establish gaps in its frameworks *Action 7 status (ongoing, extended or concluded)*: ongoing *Metrics and milestones for 2023:* ▪ the Genomics Education Programme (GEP) will undertake a desktop review of educational curricula, standards of proficiency and frameworks with a view to incorporating teaching opportunities using rare disease examples (for example, the inclusion of genomics in the Nursing and Midwifery Council standards with underpinning teaching materials developed by the GEP included in the nurse educator toolkit) ▪ there will be ongoing qualitative and quantitative monitoring and evaluation of the Rare Disease massive open online course ▪ the GEP will also continually monitor the content of the course to ensure it is up to date with the ever-evolving genomics environment ▪ the PAGE will meet twice a year, and actions and impact will be measured against the group's objectives ▪ the GEP will develop a further 2 to 5 clinical pathway initiatives (CPIs) to facilitate the integration of genomic medicine through the alignment of patient pathways, workforce development and education and/or training requirements, relating to rare diseases ▪ based on the findings of the CPI competencies and gap analysis, the GEP will also develop further tier 1 and 2 GeNotes resources relating to rare disease. **Action 8: extend the remit of the GEP to include non-genetic rare diseases** *Owner*: HEE *Progress report*: ▪ HEE has established a network of HEE Regional Genomics leads, who are linking into the Genomic Laboratory Hubs and Genomic Medicine Service Alliances system through connection with regional education and training leads ▪ HEE has established links with other HEE departments, NHS England Genomics Unit, Royal Colleges

	▪ HEE is working in partnership with the Association of the British Pharmaceutical Industry (ABPI) who will be supporting and providing expert input, where relevant, into the development of GeNotes and other GEP resource. *Action 8 status (ongoing, extended or concluded)*: extended *Metrics and milestones for 2023*: ▪ the GEP and ABPI will work together to incorporate greater understanding of future advances in medicines, including rare disease ▪ the HEE Regional Genomic leads will continue to meet 6 times a year to ensure connection to regional education and training leads ▪ 'month of genomics' activity held in collaboration with the Royal College of Obstetricians and Gynaecologists, Royal College of Paediatrics and Child Health and Royal College of Midwives to explore genetic and non-genetic rare diseases ▪ the GEP will partner with Medics for Rare Diseases (M4RD) to enhance the development of networks and resources for the rare disease hub, including those relating to non-genetic rare diseases. **Action 9: publish high-quality epidemiological and research papers to increase the understanding of rare diseases, including papers looking at basic rare disease epidemiology, impact of COVID-19 on people with some rare diseases and cancer-related risk factors or outcomes for people with some rare diseases** *Owner*: NHS Digital *Progress report*: ▪ NCARDRS has worked in partnership to contribute to 10 papers on non-cancer rare disease in 2022, which have been published, accepted for publication or are under peer review ▪ findings have been conveyed to patient groups, including Rare Autoimmune Rheumatic Diseases Alliance, Wilson Disease Support Group and the Lily Foundation; and shared on the UK Rare Diseases Forum ▪ findings have been presented at national and international conferences and events, including the 4th American Society of Haematology Annual Meeting, the Royal College of Physicians annual conference, the International Clearinghouse for Birth Defects Surveillance and Research Conference, and the Mitochondrial Medicine Conference ▪ in December 2022, a stakeholder event was held with DHSC on opportunities and challenges of rare disease registration. *Action 9 status (ongoing, extended or concluded)*: concluded *Metrics and milestones for 2023*: ▪ NCARDRS will report on the Altmetric scores on the 2022 papers in 2023 (where appropriate) as part of ongoing work under action 22 (see annex B). ***Priority 3: better coordination of care*** **Action 10: develop a toolkit for virtual consultations – improving use of videoconference and telephone clinic calls in services for patients with complex, multi-system rare diseases** *Owner*: NHSE *Progress report*: ▪ toolkit has been developed and is awaiting publication. *Action 10 status (ongoing, extended or concluded)*: ongoing *Metrics and milestones for 2023*: ▪ NHS England will make its toolkit available to all highly specialised services clinical leads.

	Priority 4: improved access to specialist care, treatment and drugs **Action 11: support rapid access to drugs for patients with rare diseases in the NHS, assessing the complexity of the service in which the drugs will be used, by mapping available access initiatives, identifying drugs and delivery challenges through horizon scanning, and listing drugs that have been identified for access** *Owner*: NHSE *Progress report*: ▪ a map of programmes has been developed ▪ NHS England is actively using the latest version of the 'preparedness template' with companies. *Action 11 status (ongoing, extended or concluded)*: ongoing *Metrics and milestones for 2023*: ▪ NHS England will produce an annual report by the end of the 2022 to 2023 financial year on access to drugs for patients with rare diseases at the point of delivery. This report will also include an analysis of overall uptake and geographical equity for those drugs recommended in the National Institute for Health and Care Excellence (NICE) Highly Specialised Technology Programme ▪ NHS England is actively working with pharmaceutical companies and providers to assess the commissioning model needed for drugs to be delivered, so that access can be provided at the point of delivery. **Action 12: develop a strategic approach for gene therapies and other advanced therapy medicinal products (ATMPs), based on horizon scanning by NHSE** *Owner*: NHSE *Progress report*: ▪ development of the strategic approach has begun but is not yet finalised ▪ NHSE has engaged with stakeholders to establish a structured approach to commissioning for ATMPs ▪ using horizon scanning, NHSE has also instigated structured proactive engagement with individual ATMP manufacturers 12 to 24 months prior to marketing authorisation. *Action 12 status (ongoing, extended or concluded)*: ongoing *Metrics and milestones for 2023*: ▪ development and implementation of the strategic approach will continue. **Action 13: capitalise on the changes made to NICE's methods and processes to ensure that NICE continues to support the rapid adoption of effective new treatments for NHS patients with rare diseases, implementing NICE's new methods and processes to support access to new treatments for rare disease patients** *Owner*: NICE *Progress report*: ▪ end-of-life criteria was replaced with a severity modifier in a methods update from February 2022 ▪ NICE accepts a higher degree of uncertainty when evidence generation is difficult, including rare diseases in a methods update in February 2022 ▪ NICE has introduced the use of the summary of information for patients – a form developed by NICE which companies complete to help support individual patient experts participate in NICE technology appraisals ▪ a refined highly specialised topic routing criteria was introduced in February 2022.

	Action 13 status (ongoing, extended or concluded): ongoing *Metrics and milestones for 2023*: ▪ all actions have been implemented as business as usual for all new treatments starting evaluations with NICE ▪ due to length of the medicines evaluation process and number of rare disease topics using older methods or processes, the analysis of the impact of changes (for example, percentage of positive NICE recommendations made following old compared with new methods and processes for rare diseases) will be available in 2023 at the earliest. **Action 14: monitor overall uptake of drugs for patients with rare diseases and map geographical access to those drugs** *Owner*: NHSE and NHS Digital *Progress report*: ▪ the standard operating procedure has been developed ▪ equity of access project is underway. Information is being gathered from a number of data sources, such as Blueteq, and locally held NHS England systems. *Action 14 status (ongoing, extended or concluded)*: ongoing *Metrics and milestones for 2023*: ▪ an annual report will be produced, and plans agreed as a way forward if access is deemed not equitable. **Action 15: map the rare disease research landscape to identify gaps and priorities for future funding** *Owner*: DHSC and Medical Research Council (MRC) *Progress report*: ▪ the project group (MRC, National Institute for Health Research (NIHR) and DHSC) developed a search protocol to identify rare disease research in the portfolios of the 2 major public funders (MRC and NIHR) over the past 5 years ▪ search results have been validated and analysed, and a report detailing the results is being prepared ▪ the outputs of this action have been delayed as data analysis has proved more challenging than anticipated. *Action 15 status (ongoing, extended or concluded)*: ongoing *Metrics and milestones for 2023*: ▪ paper published by mid-2023 ▪ continued work with industry and the charity sector to map the rare disease research funded by these organisations ▪ workshop held to identify ongoing priorities and next steps following paper publication. **Action 16: reduce health inequalities in NHS highly specialised services (HSS), including considering health inequalities at HSS annual clinical meetings, in service development and commissioning decisions, and in provider selection processes** *Owner*: NHSE *Progress report*: ▪ health inequalities are on the agenda for all the Annual Clinical Meetings for HSS ▪ a paper on geographical access was presented to the Rare Diseases Advisory Group and a standard operating procedure for undertaking the process has been developed. The exercise will be repeated every 3 to 4years ▪ a log of how health inequalities have been addressed in recent procurements has been developed ▪ NHS England has developed a draft framework and resource pack to help highly specialised commissioning teams understand and address health inequalities in procurement, which will be piloted with a few services.

Action 16 status (ongoing, extended or concluded): concluded

Annex B: summary of actions for 2023 to 2024

Priority 1: helping patients get a final diagnosis faster

Action 17: commission research on how best to measure the diagnostic odyssey
Lead organisation(s): DHSC
Outputs:
- funding call launched
- research commissioned
- metrics developed to measure diagnostic odyssey.

Outcomes:
- establish a baseline time to diagnosis
- assess effects of policy interventions on length of diagnostic odyssey
- basis for working with the NHS to identify and address challenges in delivering diagnoses faster
- identification of potential areas of health disparities.

Action-specific monitoring and evaluation:
- funding call launched in early 2023
- outcomes of the 2-stage application process by autumn 2023, with research commencing as soon as possible after contracting
- the outcome of the call, the successful research proposal, and progress made will be reported in the 2024 action plan.

Action 18: increased data-sharing for patient benefit to improve our understanding of equity of access to genomic testing and support interpretation of genomic test results
Lead organisations: Genomics England, NCARDRS and NHSE
Outputs:
- development of analytic plan for patients receiving tests against patients potentially eligible to receive a test, to investigate testing patterns and identify inequalities
- investigation of routes to share diagnostic variant data
- engagement with patient organisations to ensure patient benefit.

Outcomes:
- the regulatory framework and technical pathway for sharing data within the healthcare ecosystem will be trialled as a proof of concept
- the role of central data at this level of granularity in monitoring equity of access will be assessed.

Action-specific monitoring and evaluation:
By February 2024:
- one round of WGS data transfer from GEL to NCARDRS has taken place
- analysis plan in place at NCARDRS
- feasibility of transfer of non-WGS data from NHSE to NCARDRS assessed
- workshop held with patient organisations.

	Priority 2: increasing awareness of rare diseases among healthcare professionals **Action 19: publishing and implementing specific strategies for increasing awareness of rare diseases in the nursing and midwifery, pharmacy and primary care workforce** *Lead organisation(s)*: Health Education England (this enhances and is in addition to HEE's wider work to ensure all healthcare professionals are aware of rare disease) *Outputs*: ▪ GEP pharmacy lead in place to oversee education and training needs, including rare diseases ▪ genomics competency framework for nurses launched to address education and training (similar initiatives for midwives) ▪ rare disease case studies featured in the development of the nursing educator's toolkit ▪ GEP primary care lead contributing to Royal College of General Practitioners (RCGP) curricula review, RCGP genomics toolkit, primary care GeNotes and workforce development to include rare disease ▪ nursing and midwifery roundtable to help shape future education and training for the professionals including rare disease. *Outcomes*: ▪ improved understanding of rare diseases amongst the nursing and midwifery, pharmacy and primary care workforce ▪ A strategy outlining the approach to supporting educational and training needs for the pharmacy workforce will be published in early 2023. This work will encompass core concepts around genomics, enabling pharmacy teams to understand the application of genomics in healthcare, such as in the area of rare disease ▪ nursing and midwifery educational resources feature content on rare disease ▪ primary care education and training provision to include genomics featuring rare disease. *Action-specific monitoring and evaluation*: ▪ updated curricula to feature content on genomics and rare diseases ▪ continued engagement with stakeholders and relevant professional bodies to evaluate the uptake and impact of resources against baseline surveys of workforce in midwifery, pharmacy and primary care. ***Priority 3: better coordination of care*** **Action 20: commission research to provide the evidence needed to operationalise better coordination of care in the NHS** *Lead organisation(s)*: DHSC *Outputs*: ▪ funding call launched ▪ research commissioned ▪ evaluation of care coordination approaches complete. *Outcomes*: ▪ identification of the most cost-effective, tractable and impactful approaches to improving care coordination for people living with rare diseases ▪ evidence generated to support prioritisation of care coordination for possible future implementation within the NHS ▪ development of effective, evidence-based future policy, including facilitating policy alignment across wider government. *Action-specific monitoring and evaluation*: ▪ funding call launched in early 2023

	▪ outcomes of the 2-stage application process by autumn 2023, with research commencing as soon as possible after contracting ▪ the outcome of the call, the successful research proposal, and progress made will be reported in the 2024 action plan. **Action 21: include the definition of coordination of care in all new and revised services specifications for patients with rare diseases, and ensure the priorities of the UK Rare Diseases Framework are embedded across NHSE highly specialised services** *Lead organisation(s)*: NHSE *Outputs*: ▪ paper setting out requirements for any service specification involving patients with rare diseases to be formalised at the NHSE Specialised Commissioning Service Specification Tracking meeting ▪ new and revised service specifications include definition of care coordination ▪ priorities of UK Rare Diseases Framework discussed and reported on at HSS annual clinical meetings. *Outcomes*: ▪ increased awareness of framework priorities among commissioners and service providers ▪ HSS aligned with UK Rare Diseases Framework priorities, including coordination of care ▪ more joined up care (including access to mental health support) across HSS. *Action-specific monitoring and evaluation*: ▪ from 2023, all new and revised service specifications include definition of care coordination ▪ discussion of priorities of UK Rare Diseases Framework included as an agenda item at all HSS annual clinical meetings in 2023 ▪ progress against framework priorities reported in 2024 action plan. ***Priority 4: improved access to specialist care, treatment and drugs*** **Action 22: improved "findability" of people living with rare diseases using NCARDRS** *Lead organisation(s)*: NCARDRS *Outputs*: ▪ submission and/or publication of papers or reports describing methods to identify people with some rare diseases, including assessments on whether the methods might be applied to other diseases ▪ reporting requirements for specialised services commissioning specifications ▪ submission and/or publication of papers on descriptive epidemiology of some rare diseases ▪ public dashboard that includes information about rare disease data collected by NCARDRS, including which diseases, how it is collected and prevalence and incidence figures, where available ▪ external NCARDRS rare disease data dictionary ▪ web-based patient self-reporting system. *Outcomes*: ▪ improved national rare disease data for England, using peer-reviewed techniques that are potentially reproducible in the other countries and/or can be applied to other rare diseases ▪ improved understanding of rare diseases in England ▪ increased registration of people with rare disease to NCARDRS by NHSE specialised services ▪ increased transparency of the data that NCARDRS collects

	▪ the NCARDRS rare disease data dictionary will make clear to external stakeholders which data items may be available and/or what analysis might be undertaken for different diseases ▪ patients will be able to register themselves with the national register, so they are included in national data for their disease, ensuring "findability". *Action-specific monitoring and evaluation*: ▪ number specialised services sharing data with NCARDRS ▪ number of rare diseases with national (England) data including prevalence and incidence figures published on NDRS website ▪ number of patients who have self-registered through the new system. **Action 23: continue to improve the understanding of the impact of NHS England's specialised services commissioning activities on rare disease patients and act on this information** *Lead organisation(s)*: NHSE *Outputs*: ▪ Patient Impact Assessments (PIAs) considered in the development of all relevant commissioning policies ▪ revised Rare Diseases Advisory Group (RDAG) terms of reference for the committee to consider all policy propositions for patients with rare diseases by spring 2023 ▪ routine requests for Equality and Health Inequalities Impact Assessments (EHIA) included in provider selection exercises – from Spring 2023 ▪ examples of new Patient Reported Outcome Measures (PROMs) to be used in service specifications for patients with rare diseases. *Outcomes*: ▪ a continued and further developed process for ensuring that NHS England commissioning activities consider the impact of their activities on patients with rare diseases. *Action-specific monitoring and evaluation*: ▪ number of PIAs considered ▪ number of policy propositions considered by RDAG ▪ confirmation that all provider selection exercises for patients with rare diseases have included a request from bidders for an EHIA, and examples of how providers have addressed issues raised in the EHIA policy propositions ▪ examples of best practice in PROMs. **Action 24: establish a Highly Specialised Services Programme Board and strengthen the role of NHS England in commissioning wider services for patients with rare diseases** *Lead organisation(s)*: NHSE *Outputs*: ▪ Highly Specialised Services Programme Board established to provide assurance that services for patients with rare diseases continue to have a high profile and are of high quality ▪ extended clinical membership of the RDAG ▪ clear terms of reference for both groups to provide clarity of roles and decision-making. *Outcomes*: ▪ role of NHSE in commissioning HSS and wider services for patients with rare diseases strengthened ▪ clinical advice and clinical leadership role of RDAG strengthened

	▪ a continued focus, in light of the implementation of the Health and Care Act 2022, on highly specialised services and the Rare Disease Framework. *Action-specific monitoring and evaluation*: ▪ Highly Specialised Services Programme Board established by June 2023 ▪ terms of reference of RDAG revised by June 2023 ▪ new clinical members recruited to RDAG and given an induction. **Action 25: review the effectiveness of Early Access to Medicine Schemes, Innovative Licensing and Access Pathway and the Innovative Medicines Fund (IMF) in supporting access to treatments for people living with rare diseases** *Lead organisation(s)*: NHSE, NICE, Medicines and Healthcare products Regulatory Agency *Outputs*: ▪ report on number of applications and medicines made available through the schemes, which are treatments for rare diseases. *Outcomes*: ▪ improved understanding of the effectiveness of these schemes for improving and supporting access to rare disease medicines. *Action-specific monitoring and evaluation*: ▪ proportion of applications which are rare disease medicines reported in 2024 action plan ▪ number of rare diseases medicines progressing through the schemes reported in 2024 action plan. **Action 26: registration of national data for exemplar rare genetic conditions which cause an inherited predisposition to cancer** *Lead organisation(s)*: NCARDRS *Outputs*: ▪ outputs using the national data to possibly include publications, dashboards and data sharing of aggregate variant level data with relevant stakeholders including CanVAR-UK, DECIPHER and GEL. *Outcomes*: ▪ improved understanding of these diseases (including cancer risk), which will support better coordination of care, access to new treatments, and better outcomes for those that have them. *Action-specific monitoring and evaluation*: ▪ number of conditions with a predisposition to cancer registered. **Action 27: improving the Be Part of Research platform for people living with rare diseases** *Lead organisation(s)*: DHSC, NIHR *Outputs*: ▪ further development of the Be Part of Research platform will be informed by feedback from the rare diseases community ▪ the rare disease community will be represented on Be Part of Research's stakeholder engagement group. *Outcomes*: ▪ the Be Part of Research platform will effectively meet the needs of the rare disease community ▪ awareness of clinical research participation opportunities will be increased within the rare disease community. *Action-specific monitoring and evaluation*:

	▪ the rare disease community will be invited to take part in private beta phase testing of the Be Part of Research platform user interface by autumn 2023 ▪ outcomes of consultations with the rare disease community on the most effective way to categorise rare diseases studies on the Be Part of Research platform will be reported in the 2024 action plan. **Action 28: develop a plan to include rare diseases in NHSE'sCore20PLUS5 Framework** *Lead organisation(s)*: DHSC, NHSE *Outputs*: ▪ evidence collated to support the inclusion of people living with rare diseases in the 'PLUS' target population cohort ▪ people living with rare diseases are highlighted as a population to be identified by ICSs in the 'PLUS' target population in the 'Core20PLUS5' Framework to improve health inequalities ▪ the Core20PLUS5 Framework is applied to people living with rare diseases, to detail steps that could be taken within NHSE to address health inequalities for people living with rare diseases. *Outcomes*: ▪ people living with rare diseases recognised by NHSE as a population group that are likely to experience poorer than average access, experience and/or outcomes in healthcare services ▪ increased awareness of the inequalities in access, experience and outcomes faced by people living with rare diseases ▪ ICSs work to reduce health inequalities faced by people living with rare diseases. People living with rare diseases recognised by NHSE as a population group that are likely to experience poorer than average access, experience and/or outcomes in healthcare services ▪ increased awareness of the inequalities in access, experience and outcomes faced by people living with rare diseases ▪ ICSs work to reduce health inequalities faced by people living with rare diseases. *Action-specific monitoring and evaluation*: ▪ plan for how work will be carried out developed by autumn 2023 ▪ collation of evidence to support the inclusion of rare diseases in the 'PLUS' category to begin by winter 2023 ▪ report of the work done to support the inclusion of people living with rare diseases in the 'PLUS' target population included in the 2024 England Rare Diseases Action Plan. **Action 29: commission portfolio level evaluation of England's Rare Diseases Action Plans with input from the rare disease community on design of metrics** *Lead organisation(s)*: DHSC *Outputs*: ▪ funding call launched ▪ research commissioned ▪ metrics developed. *Outcomes*: ▪ evaluation of the influence and outcomes of the framework using metrics co-developed with rare disease community ▪ identification of potential areas of disparity ▪ development of effective, evidence-based future policy. *Action-specific monitoring and evaluation*: ▪ funding call launched in early 2023

	▪ outcomes of the two-stage application process by autumn 2023, with research commencing as soon as possible after contracting ▪ the outcome of the call, the successful research proposal, and progress made will be reported in the 2024 action plan.
Governance and organisational structures	Background on governance underpinning the development of England's action plans is covered in the first action plan and is not revisited here.
Funding model	The commitments outlined in this action plan are supported by funding for ground-breaking research, including investments of nearly £790 million into Biomedical Research Centres, and a £12 million UK rare Disease Research Platform. *Note: Leads for actions related to commissioning or funding – Actions 11, 12, 23 and 24 (NHSE), Actions 17, 20 and 29 (DHSC), and Action 15 (DHSC and MRC).* **Priority 1: helping patients get a final diagnosis faster** During 2022, NHSE developed a proposal for a SWAN pilot for people whose conditions remain undiagnosed. The model brings together multidisciplinary teams, covers all ages and aims to provide good geographical coverage across England. The model is being discussed through NHSE governance and finance structures. If relevant funding is agreed the SWAN pilot will be implemented in 2023. In the coming year, DHSC will commission policy research through an NIHR open call, inviting researchers to develop an effective method for measuring the time to diagnosis for both genetic and non-genetic rare conditions, with input from the rare diseases community. **Priority 4: improved access to specialist care, treatment and drugs** In June 2022, NHSE and NICE launched the IMF which will fast-track the most promising, cutting-edge medicines to NHS patients. Together with the Cancer Drugs Fund it represents a £680 million investment. The IMF provides faster patient access for non-cancer drugs while further data is collected. In the 2022 action plan we announced £40 million of funding for the NIHR BioResource, which works in over 50 rare disease areas to link genetic information to clinical characteristics to increase understanding of disease mechanisms for diagnostic and treatment development. In 2022, we committed to mapping the rare disease research landscape, in collaboration with the MRC and the NIHR. Analysis has now been completed for MRC and NIHR data, and a report describing the research landscape is being prepared. Wider funders sit on the project's steering group, providing insight into rare disease research across the devolved administrations, and research funded by charities and industry. Stakeholder workshops to seek feedback on gaps and priorities for future funding are planned for after publication. **The MRC NIHR Rare Diseases Research Platform** One of the major challenges in rare diseases research is being able to bring the right expertise, people and technology together for impactful research. To address this, MRC and NIHR launched a joint funding call in September 2022, to form a new UK Rare Disease Research Platform. The platform brings together challenge-led thematic nodes, with a central hub to support networking and activities that enable research. A total of £12 million is available to fund up to 10 nodes over 5 years. Outcomes of the call are expected in April 2023. **Digital, data and technology**

	A joint funding package of up to £200 million between NHSE, DHSC and the Department for Business, Energy & Industrial Strategy was announced in March 2022. Funding will support NHS research data infrastructure and data enabled clinical trials, including in genomics, and national and sub-national secure data environments.
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	*See Actions 1 and 2.*
Personalised medicine, genomics, genetic counselling	*See Actions 2, 3, 4, 6, 8, 12 and 18.* ***Annex D: supporting activities*** **Advances in genomic medicine** Published in autumn 2022, *Accelerating genomic medicine in the NHS* sets out NHSE's strategy for embedding genomics in the NHS. It details how the NHS Genomic Medicine Service (GMS) will evolve over the next 5 years to deliver a high-quality, equitable and affordable service, with priorities for improving services for the rare disease community. This includes plans to increase the capacity and capability of the workforce, including clinical geneticists and genomic counsellors. In December 2022, the Office for Life Sciences published *Genome UK: 2022 to 2025 implementation plan for England* with a range of specific actions that genomics delivery partners in England will take to implement the commitments in Genome UK. Alongside continuing roll out of whole genome sequencing in the GMS, the plan includes £105 million of government funding for Genomics England to lead the landmark research programme, in partnership with the NHS, to study the effectiveness of using whole genome sequencing to find and treat rare genetic diseases in newborns.
Models of care/care pathways	*See Actions 5, 10, 11, 16, 17, 18, 20, 21, 23, 24, 25, and 28.* **Health equity** NHS England has developed an approach called Core20PLUS5 to support NHS ICSs reduce health inequalities at both national and local levels. The approach defines a target population that would benefit from a tailored healthcare approach to improve healthcare inequalities, and identifies 5 focus clinical areas requiring accelerated improvement. 'Core20' refers to the most deprived 20% of the national population as identified by the national Index of Multiple Deprivation (IMD). 'PLUS' refers to population groups that are likely to experience poorer than average health access, experience and/or outcomes, but are not identified by the IMD. 'PLUS' population groups are determined locally by ICSs based upon national NHSE recommendations and evidence from ICS population health data. Together, 'Core20PLUS5' provides a prioritisation framework to inform the work of ICSs in improving health equity from 2021 to 2024. ***Annex D: supporting activities*** **Rare disease collaborative networks** Rare disease collaborative networks (RDCNs) are an important part of NHS England's provision to improve care, and support patients with rare diseases. The current 13 rare disease collaborative networks continue to demonstrate the breadth of work that has been undertaken by the centres, with an emphasis on collaboration and clarifying pathways for patients. Five additional RDCNs have also recently been approved, covering PTEN Hamartoma Tumour syndrome, rare bone conditions, arteriopathy and aortopathy, Bloom's syndrome and Tuberous sclerosis complex.

	Annex E: commissioning of rare disease services in NHS England The 2022 Health and Care Act marks an important step in the government's ambitious health and care agenda. The act supports a more joined-up system, ensuring that every part of England is covered by an integrated care board (ICB) and integrated care partnership, which bring together NHS, local government and wider system partners to empower them to put collaboration and partnership at the heart of planning. This new legislative framework focuses the ICBs on their local population's health, presenting an opportunity for specialised services, commissioned to care for patients with some rare conditions, to be fully integrated into the design and delivery of local pathways of care for patients. The Roadmap for integrating specialised services within Integrated Care Systems publication sets out a phased and managed approach to integrating commissioning of specialised services, currently commissioned nationally, with wider ICB commissioning responsibilities. The expectation for 2023 to 2024 financial year is that ICBs and NHSE will setup joint working arrangements overseen by a joint committee. This means that, from April 2023, they will have joint responsibility for the specialised services that have been assessed as suitable and ready for greater involvement of ICBs. It is the intention that ICBs will take on statutory delegated commissioning responsibility for these services from April 2024, subject to system readiness. Not all responsibilities will be delegated to ICBs, however, and NHSE will continue to retain responsibility for commissioning highly specialised services, where patient numbers are typically less than 500 people per year, as well as for clinical genomic services inclusive of genomic counselling.
Workforce	*See Actions 6, 7, 8, 19.*
European Reference Networks	*Not mentioned.*
EU alignment and participation	*See Action 1.* **National and international collaboration** We also engage with the Horizon Europe Partnership on Rare Diseases, due to begin in autumn 2024. To support UK input into the proposal for the partnership, we have worked with Newcastle University to establish an International Mirror and Action Group, bringing together UK researchers working on rare diseases.
Health information (including rare disease registries)	*See Actions 6, 9, 14, 16, 18, 22, 26, and 27.* ***Annex D: supporting activities*** The European Platform on Rare Disease Registration , developed by the European Commission's Joint Research Centre, aims to overcome the fragmentation of rare disease registries across Europe by making rare disease registry data discoverable, searchable and findable.(https://eu-rd-platform. jrc.ec.europa.eu/_en) The platform facilitates collaboration between registries, maximises the value of each registry's information and enables extended use of registries' data. The platform also enables pseudonymisation and data-linkage between registries, to enable encrypted and secure data transfer. Alignment, interoperability and sharing of data between registries at an international level will result in the most effective use of data arising from the rare disease community.
Orphan medicines	*Not mentioned explicitly. However, see Actions 11, 12, 13, 14, and 25.*

Rare disease research	*See Actions 1, 2, 4, 5, 9, 13, 14, 15, 17, 18, 20, 26, 27, and 29.* **Improving recruitment of trial participants** Another tool that can support people living with rare diseases to participate in research, is Be Part of Research. This is an online service that helps members of the public understand what clinical research is and what it might mean to take part, as well as showing what clinical research is currently happening across the UK. The Be Part of Research platform includes all phases of clinical trials. It draws studies from the International Standard Registered Clinical/soCial sTudyNumber and ClinicalTrials.gov registry, as well as the NIHR Clinical Research Network portfolio. It is of upmost importance that researchers list their studies on one of these public registers. The Be Part of Research website is searchable by condition and provides details of active studies, information about what the study involves, location, eligibility criteria and contact details for the researchers conducting the study. **Wider policy alignment** While the framework and action plan represent the government's primary commitments to the rare disease community, they are also closely aligned with wider initiatives, including the recently published 2022 to 2025 implementation plans for both The Future of UK Clinical Research Delivery and Genome UK. ***Annex D: supporting activities*** **UK Clinical Research Recovery Resilience and Growth** The UK Clinical Research Recovery Resilience and Growth (RRG) programme is delivering the Vision for the Future of UK Clinical Research Delivery, which sets out the government's ambition for delivering innovative, people-centred clinical research. A phase 1 implementation plan was published in June 2021, and the phase 2 implementation plan in June 2022. In the phase 2 implementation plan we committed to maintaining a rich and balanced portfolio of studies in rare and common diseases, ranging from complex, intensive studies in small, highly targeted populations to pragmatic population health research in large cohorts, and included a section on rare diseases on our RRG microsite to provide further information. The ongoing effects of the COVID-19 pandemic continues to impact on clinical research delivery in the NHS, with increased workload pressure on the NHSR&D workforce, the challenges of recovery of wider NHS services and changes to care pathways. We need to return to a situation in which new studies are able to be delivered within planned timescales. We are taking steps to address this with the aim of 80% of all open studies on the NIHR Clinical Research Network portfolio being delivered to time and target by June 2023. **Supporting clinical research in the NHS Genomic Medicine Service** The recently published NHS genomics strategy Accelerating genomic medicine in the NHS includes a number of commitments to support clinical research in genomics, of particular relevance to people living with genetic rare diseases. These include: ▪ aligning clinical trial targets with standard of care NHS testing ▪ expanding the use of NHS generated genomic data to support approved research ▪ working with patients, the public and key partners to evolve the patient choice framework ▪ putting in place mechanisms to enable the consent to, and collation of, NHS genomic sequencing data for research and innovation purposes at a national and regional level The NHS GMS Research Collaborative was established as a partnership between NHS England, the NHS GMS, Genomics England and the NIHR to facilitate and fulfil the research mission. The NHS GMS Research Collaborative aims to make it easier for researchers in academia,

	the NHS and the life sciences industry to conduct interactive genomic research and validate new genomic technologies, diagnostics and treatments to drive improvements for patients and the NHS.
Alignment beyond the healthcare sector	**Wider policy alignment** Improving the lives of those living with rare diseases goes beyond healthcare, encompassing a range of public services, including support for physical and learning disabilities. It is important these needs are considered holistically. A number of policy initiatives supporting people with disabilities have either recently been announced or are expected in the coming months (see annex D). Importantly for people living with rare conditions and their families, provision of support is based on an assessment of need, removing barriers associated with disease or diagnostic status. ***Annex D: supporting activities*** The Minister for Disabled People announced plans for a new Disability Action Plan (DAP) in December 2022. The new DAP will set out the practical actions government will take over the next 2 years to improve disabled people's lives. The policies in the DAP will be developed and consulted on over the course of 2023, so that disabled people, disabled people's organisations and other interested parties, including people living with rare diseases, can have their say. In March 2022, the Department for Education announced high needs provision capital allocations amounting to over £1.4 billion of new investment. This funding forms part of the £2.6 billion the government is investing in special educational needs and disabilities support between 2022 and 2025, and represents a significant investment in new high needs provision. It will support local authorities to deliver new places in mainstream and special schools, as well as other specialist settings, and will also be used to improve the suitability and accessibility of existing buildings. The Department for Work and Pensions expects to publish a Health and Disability White Paper in the coming months. It will respond to key areas set out in the 2021 Health and Disability Green Paper including improving services provided to disabled people, and how government can support more disabled people to start, stay and succeed in work. These new announcements are supported by existing initiatives, such as the Disabled Facilities Grant, a locally administered grant that contributes to the cost of home adaptations, including stair-lifts, heating systems and assistive technology, for eligible people to help them live safely and independently at home. The Down Syndrome Act 2022 became law in April 2022. The act aims to ensure that health, social care, education and other local authority services take account of the specific needs of people with Down syndrome when commissioning or providing services. The government made a commitment as the Down Syndrome Bill was progressing through parliament to consider whether the support needs of people with Down syndrome and people with other genetic conditions are similar. In July 2022, DHSC launched a national call for evidence to inform the development of draft guidance on the act for local authorities, which will then be subject to a full public consultation. The call for evidence sought the views of people with Down syndrome, parents and carers, professionals and people with a learning disability and other genetic conditions. The information and evidence received through the call for evidence will inform the development of the Down Syndrome Act guidance.
Any additional information (for example, background to the strategy or strategy development)	This is England's second action plan, developed with delivery partners across the health system and in collaboration with people living with rare conditions. It contains a progress report on actions from the first action plan, and details of new actions for the year ahead. Background on governance underpinning the development of England's action plans is covered in the first action plan and is not revisited here. Publication of this action plan follows our commitment to publish action plans annually during the lifetime of the UK Rare Diseases Framework. Metrics and milestones for 2023:

	▪ the UK NSC will continue work to improve the evidence available to them in evidence reviews ▪ draft manuscript on baseline comparison between UK and EURORDIS completed by spring/summer 2023 ▪ draft report on methodological principles for screening test accuracy prepared for discussion with UK NSC and Netherlands Health Council in spring/summer 2023 ▪ commissioning briefs ready for procurement in 2023. **Community engagement** People living with rare diseases are at the centre of the development of England's action plans. The rare diseases patient and clinician communities are represented on all our governance boards, and we engage with a broad range of stakeholders through the UK Rare Diseases Forum and online platform, providing opportunities for discussion and feedback. Each of our delivery partners also have their own programmes of stakeholder engagement. Input from the rare diseases community forms an integral part of all the actions listed below. In response to feedback, this year we have also undertaken a review of the forum, to ensure it remains fit for purpose, including increasing the diversity of membership and amplifying patient voice. We have partnered with Genetic Alliance UK to establish a standing, England Rare Diseases Action Plan Patient Advisory Group, which has been consulted throughout the drafting of this action plan. We have also hosted a focus group session with Breaking Down Barriers (a network of over 60 organisations working together to improve the lives of families from diverse and marginalised communities) to explore how health inequalities experienced by people from diverse and marginalised communities affected by rare conditions are being addressed in England's action plans.

Key: ABPI: Association of the British Pharmaceutical Industry; ATMPs: advanced therapy medicinal products; COVID-19: coronavirus 2019; CPI: clinical pathway initiatives; DAP: Disability Action Plan; DHSC: Department of Health and Social Care; EHIA: Equality and Health Inequalities Impact Assessments; EURORDIS: European Organisation for Rare Disease; GeNotes: genomic notes for clinicians; GEP: Genomics Education Programme; GMS: Genomic Medicine Service; HEE: Health Education England; HSS: highly specialised services; ICB: integrated care boards; ICS: integrated care systems; IMD: Index of Multiple Deprivation; IMF: Innovative Medicines Fund; M4RD: Medics 4 Rare Diseases; MRC: Medical Research Council; NCARDRS: National Congenital Anomaly and Rare Disease Registration Service; NGRL: National Genomic Research Library; NHS: National Health Service; NHSE: NHS England; NICE: National Institute for Health and Care Excellence; NIHR: National Institute for Health Research; NSC: National Screening Committee; PAGE: Patient Advisors for Genomic Education; PIA: Patient Impact Assessment; PROM: Patient related outcome measure; RCGP: Royal College of General Practitioners; RDAG: Rare Disease Advisory Group; RDCN: rare disease collaborative networks; RRG: The UK Clinical Research Recovery Resilience and Growth programme; SWAN: syndrome without a name; UK: United Kingdom; WGS: whole genome sequencing.

Table B11. Data extracted for Finland (National programme for rare diseases)

Finland	Strategy information
Author(s) **Title**	Working group on rare diseases National programme for rare diseases 2019-2023[50]
Timeline	2019-2023
Overall aim(s)	Three main themes have been highlighted in the revised National Programme for Rare Diseases: ▪ Increase expertise and its communication. ▪ Build up involvement of patients with are disease in decision-making concerning them. ▪ To establish national coordination firmly.
Themes and or priorities	Three pivotal objectives and associated areas are outlined in the strategy: **1. Increasing knowledge on rare diseases and strengthening expertise.** ▪ Increasing knowledge and awareness ▪ Strengthening the status of Rare Diseases Units and allocation of resources to them. ▪ European Reference Networks (ERN) ▪ Promoting research **2. Strengthening of patient involvement in rare disease.** ▪ Empowerment and involvement of people with rare diseases in society and their communities. ▪ Involvement of people with rare disease in developing healthcare and social welfare services in their own areas. ▪ Safeguarding the involvement of people with rare diseases in their care and services. **3. Coordination of activities related to rare diseases.** ▪ National coordination. ▪ Regional coordination. ▪ Coordination of care and services of a person with rare diseases.
Targets (if specified) and measurement method(s) (where available)	None outlined.
Implementation action(s), lead(s) and key performance indicator(s)	*The Working Group did not want to make this National Programme into a detailed list of actions. Instead, the group wanted to describe the key principles and objectives guiding decision-making to improve the position of people living with rare diseases. As changes are needed in the healthcare and social welfare services, cooperation is required between regional and national operators to implement the objectives and actions proposed in this programme. In the time when the structure and organisation of healthcare and social welfare services is undergoing a major transformation at the national level, different operators must work together to identify regionally and nationally methods to implement the objectives.*

	1.<u>Increasing knowledge on rare diseases and strengthening expertise.</u> *<u>Increasing knowledge and awareness</u>* **Objectives and proposed actions:** ▪ Increasing cooperation between website administrators producing information (for example, Duodecim, Health Village, National Institute for Health and Welfare (THL), Finnish Network for Rare Diseases (FNRD), Orphanet) to improve the availability and coverage of information in Finnish and Swedish, and to avoid overlap. ▪ Developing the content of the open hub of rare diseases in Health Village in operation with representatives of Rare Diseases Units, stakeholder organisations and association. ▪ Increasing experiential knowledge reported by people with rare diseases through cooperation between THL, development personnel of healthcare units and patient organisations. ▪ By regular surveys conducted by patient organisations assess and monitor the everyday challenges of individuals with rare diseases and flexibility of their care pathways. ▪ Improving and expanding related information on available social welfare, aids, services and guidance, and advice about its availability, in collaboration with THL, the Social Insurance Institution of Finland (Kela), Health Village and FNRD. ▪ Disseminating information on and increasing awareness of rare diseases, and organising training in cooperation with different operators in the field. ▪ Sharing through Health Village the patient information and instructions produced by the ERN in Finnish and Swedish. ▪ Ensuring continued Orphanet activities in Finland. *<u>Strengthening the status of Rare Diseases Units and allocation of resources to them.</u>* **Objectives and proposed actions:** ▪ In all university hospitals, ensuring the allocation of resources to Rare Diseases Units and consolidating their tasks and positions. ▪ Building up the knowledge base: a physician in charge and a healthcare professional with background in nursing will be needed and need to be familiar with rare diseases; it should be possible to consult a social worker. ▪ Supporting the centres of expertise and units possessing expertise in rare diseases; sharing information on available rare disease specialists. ▪ Involving the representatives of people with rare diseases in the activities of the unit and the university hospital to promote customer-oriented approaches. ▪ Communicating information on rare diseases and on unit's activities in cooperation with patient organisations and networks. *<u>European Reference Networks (ERN)</u>* **Objectives and Proposed Actions:** ▪ Nationwide, to define the duties and responsibilities of ERN centres, to create cooperation practices between an ERN and other operators in its field of expertise, to integrate ERNs into the national service system. ▪ Finland's participation in all 24 ERNs, either as a healthcare provider or an affiliated partner. ▪ With Rare Disease Units, to communicate up-to-date information about ERN centre operations to other actors in healthcare and social welfare. ▪ In collaboration with Rare Disease Units, to strengthen the role of patient organisations and representatives in the ERN application process and operations.

	▪ Agreeing on the assessment and monitoring of the national integration and other activities of the ERN centres at the national level. ▪ To develop Nordic cooperation of ERN healthcare providers and to participate in the development of European registries in cooperation with the THL and Rare Diseases Units. ▪ To ensure necessary resources and support functions for ERN healthcare providers to participate in ERN activities. *Promoting research* **Objectives and proposed actions:** ▪ To keep rare diseases research as a focus area in national research funding. ▪ To emphasise the importance of research on diseases concentrated in Finland, on their treatment and total burden to society and an individual. ▪ To keep top-notch research in Finland, increasing governmental research funding for high-quality studies on rare diseases. ▪ Targeted funding for the study of research methods used in rare diseases research. **2. Strengthening of patient involvement in rare disease.** *Empowerment and involvement of people with rare diseases in society and their communities.* **Objectives and proposed actions:** ▪ To encourage and direct individuals with rare diseases to contact relevant organisations and to seek peer support and other available services. ▪ To disseminate information on patient associations and organisations to healthcare and social welfare professionals and population in general. ▪ To promote regional and local engagement and involvement of people with rare diseases through the help of patient organisations and regional operators. ▪ To plan and implement annual Rare Diseases Days in specific catchment areas, organised jointly by the Rare Diseases Units and patient organisations. ▪ To share experiential knowledge during national and regional training days and fairs organised for social welfare and healthcare professionals, with the National Institute for Health and Welfare, the Rare Diseases Units and patient organisations. ▪ To highlight the challenges faced by people with rare diseases in Vammaisfoorumi and the Advisory Board for the Rights of Persons with Disabilities. ▪ To safeguard the operation of associated patient organisations. *Involvement of people with rare disease in developing healthcare and social welfare services in their own areas.* **Objectives and proposed actions:** ▪ To strengthen the involvement of people with rare diseases by establishing customer panels (CP) in university hospitals. CPs will convene regularly to plan and to assess contemporary issues related to healthcare and social welfare services in rare diseases, together with Rare Diseases Units, centres of expertise and other actors to reach shared apprehension of matters to be discussed with experts by experience. ▪ To plan and develop the care and service pathways of people with rare diseases jointly with healthcare and social welfare professionals, and patient organisations. ▪ To boost cooperation and communication by Rare Diseases Units to healthcare, social welfare and other professionals working with rare diseases, and to general public.

	▪ To establish regular dialogue by Rare Disease Units and patient organisations to Kela, notably about issues concerning rehabilitation, disability benefits and competitive tendering of services. ▪ To organise in all university hospitals regular annual events directed at patient organisations and people with rare diseases. ▪ To establish and develop patient feedback systems of the Rare Disease Units and ERN centres (healthcare providers): development of electronic feedback system as part of services. ▪ To define the roles of patient organisations and representatives in the operation of the ERN healthcare providers already during the application process. *Safeguarding the involvement of people with rare diseases in their care and services* **Objectives and proposed actions:** ▪ To increase guidance, advice and information about the services available provided by professionals to persons with rare diseases and about the status of patients and clients in healthcare and social welfare. ▪ To develop and strengthen group peer support through cooperation between patient organisations and healthcare. ▪ To increase and disseminate information about advisory and peer support services provided by patient organisations and associations. **3. Coordination of activities related to rare diseases** *National coordination* **Objectives and proposed actions:** ▪ Clarification of national coordination and division of labour between the Ministry of Social Affairs and Health, THL and service providers. ▪ University hospitals will strengthen regional coordination in the field of rare diseases according to the obligations of the Health Care Act and the Centralisation Decree: more detailed description of mutual cooperation and division of labour, strengthening of expertise. ▪ Integration of ERNs into our service system, cooperation with other centres of expertise. ▪ In addition to disability services, extending the general coordination tasks of THL to rare diseases. ▪ Development of registries and knowledge bases, establishing continuity of Orpha coding and other operations of Orphanet. ▪ To avoid overlap, boost cooperation and networking between the public and third sectors. ▪ Boosting cooperation in rehabilitation between the Rare Disease Units and Kela in order to design national plans for various rare disease groups. *Regional coordination* **Objectives and proposed actions:** ▪ Harmonising the regional operation of the units for rare diseases and strengthening the position of the units located in the specific catchment areas. ▪ Establishing and strengthening the cooperation of Rare Diseases Units with different healthcare units in their specific catchment areas, both in specialised medical care and basic healthcare, and communicating information about the Rare Diseases Units and centres of expertise to basic healthcare. *Coordination of care and services of a person with rare diseases.* **Objectives and proposed actions:**

	▪ Planning and piloting a case manager model to ensure seamless care and services for those people with rare diseases requiring large numbers of services. ▪ Strengthening the position of healthcare social work in the multidisciplinary cooperation carried out in the care of rare diseases. ▪ Piloting the use of personal budgets in those rare diseases that require diverse services. **Practical implementation of the National Programme and monitoring it** ▪ The Rare Diseases Units established to university hospitals play a key role in the coordination of the services required by people with rare diseases. ▪ THL has been developing national coordination of the services for persons with disabilities and the Working Group is of the opinion that many tasks in the national rare disease coordination would be suitable for THL. The role of THL as a national authority maintaining registries responds to the need for coordination in the field of rare diseases. THL has already promoted the introduction of Orpha codes. However, the maintenance of the Orphanet contact point in Finland remains to be solved. ▪ The Ministry of Social Affairs and Health focuses on enabling cross-border cooperation by promoting involvement in ERNs, enhancing the utilisation of their expertise and promoting cooperation between the Nordic countries. ▪ Patient organisations and Rare Diseases Units promote stronger patient involvement. ▪ The healthcare and social welfare professionals encountering people with rare diseases are in key positions to transmit information about available opportunities for people with rare diseases to participate in the activities of patient organisations and to access up-to-date and high-quality information. The implementation of the programme requires all parties to commit themselves to achieving the jointly drawn up objectives.
Governance and organisational structures	**Current or proposed role of different actors in the development and coordination related to rare diseases:** ▪ Ministry of Social Affair and Health - steering of legislation, resources and information, general supervision, assessment, European Union (EU) cooperation, cooperation in Nordic networks ▪ STEA (Funding Centre for Social Welfare and Health Organisations) - funding of patient organisation activities in the field of rare diseases, assessment of effectiveness of such measures ▪ Healthcare and social welfare - production of services, improving the availability of expertise, agreeing on service pathways and referral practices ▪ University Hospital Districts - regional cooperation and coordination tasks in accordance with the Centralisation Decree (582/2017), information production to Health Village, international research activities, coordination of centres of expertise and ERN healthcare providers, care instructions ▪ National Institute for Health and Welfare (THL) - information guidance, maintenance of networking, project steering, comprehensive research, assessment and maintenance of services, functioning measures, Orpha codes, knowledge-bases and registries ▪ COHERE Finland - knowledge steering, assessment of inclusion of services and treatments in rare diseases in the service palette of national healthcare ▪ Social Insurance Institution of Finland - reimbursement of medicines, costs of cross-border care, other benefits and services, rehabilitation ▪ Fimea, Pharmaceuticals Pricing Board (Hila) marketing authorisation of medicinal products, assessment of benefits to treatment from orphan drugs, conditions for reimbursement of medicines (Hila) ▪ Finnish Network for Rare Diseases - to influence matters promotion of joint lobbying of organisations, communication, compiling and disseminating information

	▪ HARSO (an umbrella organisation of associations supporting patients with rare diseases and disabilities) - promotion of organisations' joint activities to influence matters ▪ Norio Centre of Rare Diseases - maintenance of the Finnish Orphanet website, international cooperation.
Funding model	**The strategy estimates that approximately 1.6 additional person-years would be needed for physicians and 0.8 person-years for nurses at the national level. The cost effect would be approximately EUR 200,000 per year.** National coordination requires personnel resources in the national coordination unit. According to Subcommittee calculations, at least two person-years are required for the national coordination tasks, including the communication of information, coordination of networks, update and maintenance of the Orpha codes, and Orphanet activities. Resources are also required for development of the database and the maintenance of registry for rare diseases. In total, these amount to EUR 200,000 - 300,000 per year. The European Commission grants the ERN centres operating in Finland a small amount of financial support for ERN activities. For healthcare providers to fulfil the quality requirements for ERN centres, an additional amount between EUR 20,000- 40,000 per year is needed, for maintenance of required procedures and quality systems. Participation in an ERN uses an input equal to 0.1 person-years for each sub-group in the network. In total, there may be up to ten of them. If centres of expertise joined all the 24 ERNs during the programme period, the number of Finnish centres would total approximately 30. The total amount of work would be between 20 and 25 person-years, divided between several specialists. The imputed costs are about EUR 2 million per year. It has been estimated that an input of less than EUR 1 million is used to maintain the necessary systems in the year a centre is established and about half of that in the following years. **Research funding and research cooperation (Extracted from section Implementation of programme objectives in 2014-2017 and changes in operational environment)** Finland has conducted no comprehensive study of research focusing on rare diseases. According to the estimate by the Academy of Finland in 2017, the Academy's Research Council for Biosciences, Health and the Environment had granted just over EUR 20 million to 57 research projects focusing or touching upon rare diseases between 2011 and 2017. Excluding research in rare cancers and infectious diseases, the overall funding for research in rare diseases was EUR 19 million. This is less than 10% of funding from the Research Council. Of the 24 rare disease groups included in the ERNs, 10 research fields remained completely unsupported during the time of the estimate, despite internationally effective research in many of them. These disease groups include also diseases enriched in Finland. There are other funding sources for research conducted on rare diseases in ERN centres and universities. In the total funding, the importance of short-term funding from research foundations has increased while – due to cuts in government research funding – the number of research personnel has reduced and fewer research equipment updated. Research focusing on the genetics and epigenetics of rare diseases requires that genomic variation be reliably and precisely determined, especially in populations with a narrow genetic base. A significant part of scientific research in rare diseases also focuses on patients identified during clinical practice in university hospitals and on the ensuing translational studies collaboratively carried out by the clinician and basic researchers. In such studies, continuous governmental research funding granted to hospital districts plays a vital role. In 2013, the Academy of Finland joined the International Rare Diseases Research Consortium (www.irdirc.org). The consortium brings together actors whose work involves rare diseases research. Furthermore, the Academy has participated in the European E-RARE-3 research funding cooperation between 2017 and 2018. In 2019, a five-year funding project by the European Commission, the European Joint Programme on Rare Diseases (www.ejprarediseases.org) will be launched. The objective of this project is to improve the quality of life

	for individuals with rare diseases by increasing knowledge about the diagnostics, treatment and care of rare diseases. The project brings together research sponsors, research institutes, universities, university hospitals, ERN Centres of Expertise and patient organisations. The Academy of Finland has participated in this from its beginning. Rare diseases have been the object of international clinical pharmaceutical research projects, while Finland's participation in them, and in pharmaceutical research in general has declined. The Virtual Hospital 2.0 project (2016-2018) of the five university hospitals is funded by the Ministry of Social Affairs and Health. **3.2.1 Empowerment and involvement of people with rare disease in society and their communities.** There are dozens of associations and organisation representing people with rare diseases in Finland. The Finnish Network for Rare Diseases, consisting of 20 associations, is a national cooperation network of various health and social welfare organisations in the field of rare diseases. HARSO is an umbrella organisation of associations supporting patients with rare diseases and disabilities. Consortiums of organisations and associations lobby matters concerning people with rare diseases at the national level. Information on organisations, associations and interest groups representing people with rare diseases is available on the Finnish Network for Rare Diseases website (www.harvinaiset.fi). Each of these represents its target group and lobbies issues important to them and to everyone with rare diseases. Several receive support from STEA. It channels net revenue from the Finnish gaming company Veikkaus. Enabling support to small associations and to rare disease patients without any remains challenging.
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	*Not mentioned.*
Personalised medicine, genomics, genetic counselling	To implement the health sector growth strategy, four National Centres of Excellence that have been highlighted as key strategic focus areas are in the process of being established in Finland. The goal of a project entity aimed at better utilisation of genomic data is to establish a national Genome Centre. Legislation in the use of genomic data and legislative clarification of the status of biobanks is currently in preparation. Among other things, biobanks collect and store biological samples for rare disease research. In addition to five regional cancer centres, a national cancer centre (Comprehensive Cancer Centre Finland) has started in 2019 while the establishment of a Neurocentre Finland is in preparation. These projects will improve the operating conditions of personalised medicine in healthcare. Personalised medicine plays an important role also in the treatment of rare diseases.
Models of care/care pathways	As there are very few evidence-based clinical practice guidelines for rare diseases, guidelines for diagnostics, care and service pathways should be formed through cooperation and consideration the experience gained by different operators. The ERNs produce information on the diagnostics and treatment of diseases in their own disease groups and promote rare disease-focused scientific research. The Finnish centres of expertise participate in this. Such information should be utilised when creating national practices. Medical information is supplemented with information about social welfare services on disease- or disease group-specific basis. General knowledge about social welfare services does not always suffice when services for an individual with rare disease are designed. The Health Village hubs for rare diseases and rehabilitation (www.kuntoutumistalo. fi) contain information on social welfare services, among other things. The care and service pathways of people with rare diseases vary according to disease characteristics and the person's life situation. To better enable people with rare diseases to timely receive the needed treatments, individualized care and service pathways should be designed. Such a pathway describes the key procedures, issues and operators for which individuals' needs should be considered and availability ensured

	while organising their care and services. For the largest and especially challenging groups of rare diseases, on top of general descriptions diagnostic and care instructions which include general quality requirements and list special challenges at different stages of the care and service pathway will be needed. Such pathway descriptions should be delineated in collaboration with patient organisations and networks. The challenges in everyday life vary between different rare diseases. One therefore will need to describe in disease-specific ways how coping with everyday life could be supported best. The nature of social support needed will likely vary in different rare diseases. **National coordination** The establishment of a national coordinating centre was proposed in the first National Programme none has been implemented. Some coordination has been performed by the Working Group on Rare Diseases and its Subcommittee. One of the tasks of the current Working Group is to propose a model for national coordination. During the update of the National Programme, our understanding of the importance of national coordination in the development of care and comprehensive support of people with rare diseases has been reinforced. In the surveys conducted, rare disease associations, the Rare Diseases Units and ERN centres all supported the establishment of a coordination centre almost unanimously. The importance of national coordination was stressed in many of the speeches held in the National Conference on Rare Diseases in autumn 2018. A variety of tasks have been proposed for the coordinating centre, including gathering information on rare diseases and promoting the networking of operators in the field of rare diseases. Tasks could include systems research related to rare diseases and surveys of needed services, for example by utilising registry data. Management of the overall status of rare diseases would be improved by a national database tagging rare diseases. Presently, there are occasional registries of individual rare diseases or disease groups. The Rare Diseases Units and the THL are jointly developing the possibility to add not only the ICD-10 but also the exact Orpha code to the diagnosis sections of electronic health records. A national rare diseases registry would enable to combine the data to EU and ERN registries. Without international registries, the diagnostics, care and monitoring of ultra-rare diseases cannot be developed adequately. The legislative amendment concerning national THL quality registers would permit the creation of such national registry. Table 4 describes various proposals for rare diseases, inclusive of bolstered coordination tasks of THL. **Regional coordination** University hospitals bear the regional responsibility for, plan and coordinate the prevention, care, diagnostics and rehabilitation of rare diseases. The clinical units and centres of expertise responsible for the diagnostics and care provide the services required by people with rare diseases in their field of specialisation. If necessary, the services are provided in multidisciplinary and multiprofessional cooperation. The tasks of the Rare Diseases Units include participation in the coordination of the diagnostics and the range of services provided to people with rare diseases, advising and referring them to the right experts and to the proper care or service pathway, supporting the clarification of the care and service pathways in their own specific catchment area, and cooperation with different healthcare units, authorities and organisations. The units' task is to help create smooth consultation and referral opportunities and to participate in the coordination of the care and diagnostics of those patients who have symptoms consistent with rare diseases but for whom no diagnosis has been found in basic or specialised medical care. Consultation models for improving the diagnostics, care and coordination of the care of rare diseases may be developed in the electronic development projects in the field of healthcare and social welfare. University hospitals can establish centres of expertise for groups of rare diseases or gather diverse professional working groups, for which they find the required expertise and through which they collaborate regionally or nationally with other parties providing care. The tasks of the Rare Diseases Units do not include outpatient clinic activities as the examinations and care choices are the responsibility of various specialist units of the university hospital districts. If necessary, these consult the ERN healthcare providers or refer the patients to them. The care of patients in a stable phase can also be implemented in other healthcare units in the area, as long as sufficient consultation support is available.

Workforce	**Strengthening the status of Rare Diseases Units and Allocation of resources to them.** In accordance with the Government Decree on the Division of Work and Centralisation of Certain Tasks (582/2017, section 4), rare diseases units were established in each of the five university hospitals, between 2015 and 2017. A physician in charge and a healthcare professional with background in nursing work in each unit. The Rare Diseases Units (Centres) have developed at different paces, according to their resources. To promote equity at the national level, it will be necessary that the basic tasks of the units be determined in a uniform manner, to further delineate the obligations laid down in the Centralisation Decree. However, due to regional and hospital-specific differences, unit activities include different tasks and focus areas. See Focus Area 1, objective - disseminating information on and increasing awareness of rare diseases, and organising training in cooperation with different operators in the field. See Focus Area 2, objective - to share experiential knowledge during national and regional training days and fairs organised for social welfare and healthcare professionals, with the National Institute for Health and Welfare, the Rare Diseases Units and patient organisations.
European Reference Networks	**Units and centres of expertise for rare diseases (Extracted from section Implementation of programme objectives in 2014-2017 and changes in operational environment)** The establishment of Rare Diseases Units in all five university hospitals and the membership of a total of 14 centres of expertise from four university hospitals as healthcare provider representatives in the ERN for Rare and Low Prevalence Complex Diseases have been important reforms in promoting the diagnostics and treatment of individuals with rare diseases. The status of Rare Diseases Units (and/or Centres) has been strengthened with the Governmental Decree on Centralization of Specialist Health Care and Some Other Actions (582/2017). For their part, these measures have improved the status and involvement of individuals living with rare diseases. The importance of the status and tasks of these units and centres is emphasised in the objectives and proposed actions of this National Programme. In 2014, the European Commission set up criteria according to which a healthcare unit can apply to the European Reference Networks (European Reference Networks for Rare and Low Prevalence Complex Diseases, ERN; https://ec.europa.eu/health/ern_en). The catalyst for establishing ERNs was the EU Directive (2011/24) on the application of patients' rights in cross-border healthcare. Aims of ERNs were to empower choices to care pathways, organise joint training and consultations, and to enable cross-border discussions on the situation of a person with rare diseases without need to travel to another country, apart from few exceptional cases. Expertise in each network relates to its specific group of rare diseases. Eurordis, an umbrella organisation of European rare disease patient organisations, participated in establishing criteria for ERN healthcare providers (www.eurordis.org). Strengthening of patient involvement in the operations of ERNs and its healthcare providers was among the objectives. In 2017, 24 networks started their operations in Europe. More than 900 different healthcare providers from 25 Member States and Norway participate. In 2018, 14 units from four Finnish university hospitals are members of 12 different ERN. Active participation in the ERNs by Finnish university hospitals will promote expertise in rare diseases and development of patient care. Aim will be to have at least one university hospital representative in each reference network. **Increasing knowledge on rare diseases and strengthening expertise (objective of the National Programme 2019-2023).** Strengthening rare disease expertise and increasing accessibility of information provide ways of improving the diagnostics and care of rare disease patients. As part of cross border healthcare, increasing the availability of information and expertise in rare diseases has been entrusted to ERNs. In addition to the ERN healthcare providers, further units and centres of expertise in rare diseases also operate in

	hospital districts. To find best available expertise, nationwide cooperation and sharing of information will be pivotal. Critically, scientific research increases expertise and makes the development of new treatments possible. *See Objectives and proposed actions for ERNs (implementation actions).*
EU alignment and participation	**Disseminating information and strengthening knowledge** The Rare Diseases Units have organised training for healthcare professionals in their own specific catchment areas. Rare diseases have been introduced in medical journals, at physician's seminars in different regions and at conferences and events organised by different stakeholders. The Nordic Conference on Rare Diseases was held in Finland 2014. Finnish actors from the field of rare diseases have participated in the Nordic Conference on Rare Diseases in Copenhagen in 2016 and in the conferences of Eurordis. Eurordis conferences are held every two years; the most recent one was held in May 2018 in Vienna. Finland also participates in the Nordic Network on Rare Diseases aimed at promoting Nordic cooperation in the field of rare diseases. The network is funded by the Nordic Council of Ministers. The network of Nordic patient organisations promotes cooperation between groups representing people with rare diseases.
Health information (including rare disease registries)	*See increasing knowledge and awareness (implementation actions).* **National registry for rare diseases and streamlining of care pathway (Extracted from section Implementation of programme objectives in 2014-2017 and changes in operational environment)** Establishing a National Rare Diseases Registry has been promoted through cooperation between the THL and the Rare Diseases Units in university hospitals. The Orpha nomenclature, based on the diagnosis database of the European Orphanet website (www.orpha.net) collecting data on rare diseases will be integrated with the Finnish code server parallel to the ICD-10 disease classification. The codes will make the identification of rare diseases easier. There are also plans to make Orpha codes a part of the Care Register for Health Care. A project to design alerts for those rare diseases in which special vigilance or expertise is required from healthcare professionals is ongoing; such alerts should be implemented into all electronic patient record systems in use. To enhance the diagnostics, care and rehabilitation of rare diseases and to promote service provision, information about these has been made available in the professional section of the Health Village rare diseases hub. However, adequate information on available rare disease rehabilitation and social welfare services covering all levels of the service system is still lacking. The ERNs have started to produce information and guidance on the treatment of rare diseases. These can also be used nationally. **National coordination** Management of the overall status of rare diseases would be improved by a national database tagging rare diseases. Presently, there are occasional registries of individual rare diseases or disease groups. The Rare Diseases Units and the THL are jointly developing the possibility to add not only the ICD-10 but also the exact Orpha code to the diagnosis sections of electronic health records. A national rare diseases registry would enable to combine the data to EU and ERN registries. Without international registries, the diagnostics, care and monitoring of ultra-rare diseases cannot be developed adequately. The legislative amendment concerning national THL quality registers would permit the creation of such national registry.
Orphan medicines	*Not mentioned.*

Rare disease research	**See Promoting research (and associated objectives and actions)** Research enables the development of more specific diagnostics and new treatments in rare diseases. Essential knowledge on the prognoses of rare diseases, on their treatment options, associated diseases and effectiveness and necessity of screening for these is lacking. Even less information is available on issues related to rare diseases like the extent of decline in the quality of life, on the efficiency of non-pharmaceutical therapies, on the burden to healthcare and social welfare or the total costs of rare diseases to people suffering from them and to their families. Some of these rare diseases are a part of the Finnish Disease Heritage, while novel and rare inherited diseases, which are less prominently concentrated in our population are being discovered constantly. There is dire need for comprehensive research data on the total burden to society and to individuals caused by these diseases. While Finnish researchers participate in many international research projects, the greatest challenge to Finnish rare diseases research has become that researchers move abroad towards better funding opportunities, mainly to other Nordic, Central European or Northern American countries. The establishment of the European Reference Networks will likely increase international research cooperation. However, any Europe-wide research funding potentially received will often be divided between multiple centres in different countries. It will be especially challenging to obtain European research funding for diseases specifically enriched in Finns. Funding of rare diseases research should therefore remain a focus area in national funding. Rare diseases research is important not only to augment knowledge on rare diseases but also to understand the development of common non-communicable diseases. By providing unique information on the normal functioning of the human body at molecular level, rare diseases research enables us to model disturbances in the function of the organs and cells and to pinpoint pathogenetic mechanisms in more common diseases.
Alignment beyond the healthcare sector	**Coordination of care and services of a person with a rare disease** The importance of the planning of care and services is emphasised in situations when multidisciplinary services are needed but available information is scarce. A comprehensive customer plan makes it possible to provide many people with rare diseases with adequate support for smoothly daily life. The expertise of healthcare social workers and rehabilitation instructors should also be used when drawing up a plan: a comprehensive plan should include both the healthcare and the social welfare services. When drawing up the plan, advantage should be taken of the expertise of the Rare Diseases Units, ERN centres, organisations and associations, as necessary. According to the Social Welfare Act (1301/2014, section 42), a case manager must be designated to a client if the client's need for services is not short-term or temporary. The objective of the INNOVCare project funded by the EU was to develop structural reforms and comprehensive and customer-centred service pathways improving the social support of people with rare diseases. The project ended in 2018. It emphasised the importance of a case managers supporting people with rare diseases and their families in the coordination of the services and in facing the challenges of everyday life. The case manager helps to find the local experts, works as a contact person for local and national expertise and gives empowering support to persons with rare diseases and the family members. Based on the experience gained in the project, consideration should be given to when it is important to designate a case manager to a person with rare diseases, in which tasks the role of the case manager should be used and how the case manager could best support the person's involvement in his or her care and service pathways. *See above "objectives and proposed actions for coordination of care and services of a person with a rare disease.* "
Any additional information (for example, background to the strategy or strategy development)	**Strategy Development** The National Programme was drafted in the Sub-Committee of the Working Group on Rare Diseases, established by the Ministry of Social Affairs and Health. We would like to thank the Sub-Committee for its invaluable work. The Programme was edited by a representative of the Finnish Network for Rare Diseases, Risto Heikkinen from the Finnish Federation for Allergy, Skin and Asthma. All key stakeholders have commented on it before publication.

	In spring 2018, the Working Group decided to update the National Plan for a four-year period, as proposed by the Sub-Committee. Risto Heikkinen, a member of the working group, was chosen for the task of coordinating the update and writing the revised programme. Individuals with rare diseases, their families and key professionals from the field of rare diseases were involved in the update. A survey to organisations and associations representing rare diseases was conducted during autumn 2018. A patient advocacy group and other member communities of the Finnish Network for Rare Diseases (www.harvinaiset.fi), consisting of 21 social and health organisations, were in various ways involved in evaluating the implementation of the first National Programme and in updating it. In addition, a survey to the five Rare Disease Units in university hospitals and to the 14 Finnish healthcare provider members of ERN networks was conducted. The discussions and results from the national conference on rare diseases organised in October 2018 further complemented the programme. Before its finalisation, the updated draft programme was sent to the stakeholders for comments. The first Finnish National Programme for Rare Diseases 2014-2017 followed the recommendations of the Council of the European Union. The programme detailed a plan for various necessary actions, but not all of its objectives were accomplished. Three main themes have been highlighted in the revised National Programme for Rare Diseases: the involvement of people with rare diseases, augmenting expertise and strengthening coordination. These themes are examined at different levels of the Finnish service system. This Programme is not a detailed action plan, but it rather outlines the general direction for decision-makers and people working with rare diseases, who on their behalf are responsible for the measures and monitoring of this programme during its implementation. **Proposed actions 2014-2017** ▪ Adopting a uniform definition for rare diseases and acknowledging the need for dedicated measures ▪ Establishing a national registry for rare diseases ▪ Focused research funding and research programme for rare diseases ▪ Strengthening of international research collaboration ▪ Streamlining the care pathway for an individual with rare disease ▪ Establishing Units for Rare Diseases in all university hospitals ▪ Establishing specialized Centres of Expertise for Rare Diseases ▪ Providing more education and training ▪ Promoting the availability of orphan drugs ▪ Establishing a national coordinating centre for rare diseases ▪ Systematic collection and sharing of information ▪ Developing social support and rehabilitation ▪ Augmenting rare disease patient involvement. **Observations on the implementation of the first programme objectives.** ▪ On a general level, the programme strived towards the identification of development areas and recording the challenges affecting the life of individuals suffering from rare diseases. ▪ The implemented actions were those that were achievable by developing or changing existing operations. ▪ The measures requiring national agreement have been implemented only partially.

	▪ As of now, the needs of individuals with rare diseases have been insufficiently acknowledged in legislation to for example enable equitable care pathways. ▪ Actions requiring new resources, or redivision of resources or funding, were largely not implemented.

Key: CP: customer panels; ERN: European Reference Networks; EU: European Union; Eurordis: European umbrella organisation of rare disease organisations; FNRD: Finnish Network for Rare Diseases; HARSO: an umbrella organisation of associations supporting patients with rare diseases and disabilities; Hila: Pharmaceuticals Pricing Board; Kela: the Social Insurance Institution of Finland; STEA: Funding Centre for Social Welfare and Health Organisations; THL: National Institute for Health and Welfare.

Table B12. Data extracted for France (French National Plan)

France	Strategy information
Author(s) **Title**	The Ministry for Solidarity and Health and the Ministry for Higher Education, Research and Innovation. French National Plan for Rare Diseases 2018-2022[51]
Timeline	2018-2022
Overall aim(s)	The aim is to drive a national momentum, underpinned by key measures that should lead to important improvements in terms of diagnosis, care provision, our understanding of these diseases and the development of effective treatments. More specifically, this strategy aims to: ▪ Make sure each patient receives a faster diagnosis and reduce diagnostic delay, with a quantified objective reduced to 1 year ▪ Reinforce the structuring of databases in order to increase research potential ▪ Boost the role of clinical networks to coordinate the actions of the multiple players concerned and support certain key phases, such as delivery of the diagnosis ▪ Ensure greater clarity of the care pathway for both patients and their families ▪ Encourage innovation and make it accessible ▪ Put in place new neonatal screening programmes ▪ Reinforce France's role as a driving force in Europe. The strategy is hinged around three ambitions: ▪ to enable a rapid diagnosis for all in order to reduce diagnostic delays and undiagnosed diseases ▪ to innovate in order to treat ▪ to improve the quality of life and care pathway of patients. And two levers: ▪ communication and training ▪ modernisation of organisations and national funding mechanisms. The main quantitative objective is: to ensure all people living with a rare disease receive an accurate diagnosis, care, and available therapy within one year of their first specialised medical consultation.
Themes and or priorities	**Abbreviations used throughout the strategy:** ABM - Biomedicine Agency AFCG - Association of Genetic Counsellors AFM- Myopathies Association MA - Marketing Authorisation AMR - Rare Diseases Alliance ANR - National Research Agency

	ARIIS - Alliance for Health Industry Research and Innovation ARS - Regional Health Agency ATHENA - National themed alliance for human and social sciences ATU - Temporary authorisation for use AVIESAN - Alliance for Life and Health Sciences DB - Database BNDMR - National rare disease data bank BPI - French Public investment bank CCMR - France Rare disease competence centre CCNE - Ethics committee CIC - Clinical Investigation Centre CNAMTS - National health insurance fund for employed workers COPIL - Steering committee CRDN - Regional neonatal screening centre CNEDIMTS - National medical device and health technologies assessment committee CNSA - National Solidarity Fund for Independent Living CPDPN - Multidisciplinary prenatal diagnosis centre CRMR - Rare disease reference centre CSF - Health industries and technologies sector committee CSIS - Health industries strategic council DGCIS - Directorate General for Competitiveness in Industry and Services DGCS - General Directorate for Social Cohesion DGEFP - General delegation for employment and professional training DEGESCO - General Directorate for School Education DGOS - General Directorate for Healthcare Services DGRI - Directorate General for Research and Innovation DGS - General Directorate of Health DGESIP - General Directorate for Higher Education and Professional Integration DMP - shared medical record DNN - Neonatal screening (NNS) DPC - Continuing professional development DPI - Preimplantation genetic diagnosis (PGD) DPI - Computerised patient record DPN - Postnatal screening DRC - Clinical research department DSS - Directorate for Social Security ECRIN - European clinical research infrastructures network ERHR - "Rare disability" relay team EJP - European joint program ETP - Patient education

	EUCERD - European Union committee of experts on rare diseases EURORDIS - European organization for rare diseases ERN - European Reference Network FCRIN - French clinical research Infrastructures Network FMR - Rare Diseases Foundation FSMR - Rare disease clinical network FUI - Single Interministerial Fund HAS - French National Authority for Health HCERES - High Council for assessment or research and higher education HCSP - High Council for public health IHU - University Hospital Institute IMI - Innovative medicines initiative INSERM - National Institute for health and medical research IRDIRC - International rare diseases research consortium ITMO - Multi-organisation themed institute ITMO - GBB Multi-organisation genetics, genomics and bioinformatics institute Leem - Pharmaceutical companies' representative body LMD - Degree-Masters-Doctorate (DMD) MDPH - level centres for disabled people MESRI - Ministry of Higher Education, Research and Innovation MIG- funding for work "in the general interest" MRIS - Rare Diseases Info Service NGS - New-generation sequencing OMEDIT - Observatory for medicinal products, medical devices and therapeutic innovation PFMG - France Genomic Medicine 2025 plan PHRC - Clinical research hospital programme PIA - Investments for the Future Programme SME - Small and medium-sized enterprises PNDS - National care and diagnosis protocols FEFIS - French Federation of health industries PREPS - Research programme on healthcare system performance PRME - Medico-economic research programme PRS - Regional health project PSPC - Key research and development projects for competitiveness Radico - Rare disease cohorts RCP - multidisciplinary consultation meetings RHU - University hospital networks RGPD - General data protection regulation ROR - Operational resources directory RTU - Temporary recommendation for use

	SATT - Technology transfer acceleration company SDM - MR Minimum data set for rare diseases SHS - Human and social sciences SIDIV - Union for the in vitro diagnostics industry SIGAPS - System to search, manage and analyse scientific publications SI SAMU - Information system for the emergency medical assistance service (SAMU) SPIS - Public health information service SNITEM - National medical technologies industry trade association EU - European Union UNDI - Undiagnosed diseases network international URC - Clinical research unit **11 focuses (with associated objectives and actions) are outlined in the strategy:** **Focus 1: Reducing diagnostic delays and undiagnosed diseases** **Focus 2: Improving neonatal screening and prenatal and preimplantation diagnostics to enable earlier diagnoses** **Focus 3: Sharing data to aid diagnosis and the development of new treatments** **Focus 4: Promoting access to treatments in rare diseases** **Focus 5: Giving new momentum to research in the field of rare diseases** **Focus 6: Promoting the emergence of and access to innovation** **Focus 7: Improving care pathways** **Focus 8: Facilitating the integration of people with rare diseases and their carers** **Focus 9: Training health and welfare professionals to better identify and manage rare diseases** **Focus 10: Reinforcing the role of rare disease clinical networks in care and research issues** **Focus 11: Specifying the positioning and missions of other national players in the field of rare diseases** ▪ **Focus 1: Reducing diagnostic delays and undiagnosed diseases** ***Objectives:*** ○ to structure and harmonise diagnostic strategy in order to reduce diagnostic delays ○ to regularly reassess the cases of currently undiagnosed patients in order to obtain a diagnosis in light of scientific advances. ▪ **Focus 2: Improving neonatal screening and prenatal and preimplantation diagnostics to enable earlier diagnoses.** ***Objectives:*** ○ to increase the number of diseases screened for as part of the national neonatal screening programme ○ to accelerate the implementation of new neonatal screening tests ○ to reinforce resources for PND and PGD depending on requirements ○ to tackle the ethical and regulatory issues raised by PND and PGD and the performance of postnatal screening in the general population, in the context of revision of the bioethics law. ▪ **Focus 3: Sharing data to aid diagnosis and the development of new treatments.** ***Objectives:***

	○ the deployment of the national rare diseases data bank (BNDMR), which will collect a minimum data set for all CRMR patients ○ the development of FAIR data warehouses, interoperable with European or international data warehouses ○ the implementation of conditions for the reuse of data collected using e-health tools for research in the field of rare diseases. ▪ **Focus 4: Promoting access to treatments in rare diseases.** ***Objectives:*** ○ to promote rapid access by patients to therapeutic innovations that are already authorised or in the process of being so ○ to reinforce real-life knowledge of medicinal products authorised in the treatment of rare diseases ○ to have access to a regularly updated inventory of therapies (medicinal products, medical devices, non-medicinal treatments) offered to patients in the treatment of rare diseases, be they products in the development pipeline, medicines or products prescribed outside the authorised framework, medical techniques, in order to be able to detect new substances of interest, substances to be repositioned, to identify interesting proofs of concept, off-label uses, non-medicinal approaches or development or investment needs ○ to attempt to regulate off-label prescribing practices by establishing a temporary authorisation for use (RTU) when the available data are deemed to be insufficient by the ANSM or, failing this, improve knowledge of these practices. ▪ **Focus 5: Giving new momentum to research in the field of rare diseases.** ***Objectives:*** The objective is to give fresh impetus to research in the field of rare diseases in France and to reinforce the country's role as a European leader in order to reduce the number of patients without a diagnosis and accelerate the development of new treatments: ○ by coordinating the participation of national players in European fundamental, translational and clinical research programmes in the area of rare diseases ○ by launching a French research programme focusing on undiagnosed diseases ○ by developing human and social sciences-based research into rare diseases. ▪ **Focus 6: Promoting the emergence of and access to innovation.** ***Objectives:*** The objectives are to promote the more rapid development of innovative diagnostic products or treatments, as well as the repositioning of drugs and their market access: ○ by establishing an innovation coordinating body tasked with defining new innovation strategies for rare diseases ○ by facilitating access to market of innovations for rare diseases ○ by proposing specific research and development mechanisms in the field of rare diseases. ▪ **Focus 7: Improving care pathways.** ***Objectives:*** ○ create accompaniment phases to enable medical, care and psychosocial support teams to more effectively manage and adapt certain key moments in the patient care pathway and provide tailored, progressive and respectful information. There will be a particular focus on diagnosis delivery, follow-up in the event of an undiagnosed disease and the transition from adolescence to adulthood ○ organise emergency situations without disruption to the care pathway ○ incorporate patient education programmes in the care pathway, enabling patients to be more active and autonomous in their own care

	○ facilitate communication between players to improve coordination of the care path, identifying designated contact persons for patients and developing facilitator technical tools. ▪ **Focus 8: Facilitating the integration of people with rare diseases and their carers.** ***Objectives:*** Improve the quality and continuity of life paths and access to medico-social mechanisms, reinforcing the link between the public health and medico-social approach in order to: ○ facilitate access to mechanisms, rights and services aimed at disabled people and their carers ○ organise partnerships with the "rare disabilities" mechanism ○ encourage the development of health autonomy support projects specific to rare diseases ○ take into account the specific situations of people with rare diseases in their educational and professional pathways. ▪ **Focus 9: Training health and welfare professionals to better identify and manage rare diseases.** ***Objectives:*** ○ specify the role of new professions liable to improve the diagnostic care of patients (genetic counsellors, bioinformatics specialists, etc.) and increase the training and number of these professionals ○ adapt the initial and continuing training of health and social professionals in order to promote a "culture of questioning" and knowledge of the healthcare organisation system in France for the management of rare diseases. ▪ **Focus 10: Reinforcing the role of rare disease clinical networks in care and research issues.** ***Objectives:*** The FSMRs care and research coordination missions on care and research of the FSMR will be reinforced, in particular, by the collection and sharing of data, in relation with national mechanisms to support research and set up collaborative spaces for targeted actions promoting exchange between entrepreneurs, healthcare professionals, patients and regulatory players. In order to coordinate their approaches, the steering committee (COPIL) of the clinical networks will be responsible for setting their organisational, strategic and operational priorities. While maintaining their specific characteristics, they will therefore ensure complementarity and cross-functionality in order to pool actions and resources to address the multi-system symptoms and consequences of numerous diseases. FSMR representatives will be members of the strategic committee and the operational committee of the PNMR3. ▪ **Focus 11: Specifying the positioning and missions of other national players in the field of rare diseases.** ***Objectives:*** The objective is to specify the positioning and missions of these national players to better incorporate them with the rare diseases ecosystem and optimise their impact.
Targets (if specified) and measurement method(s) (where available)	▪ To enable a rapid diagnosis for all in order to reduce diagnostic delays and undiagnosed diseases; ▪ To innovate in order to treat, so that research increases therapeutic resources; ▪ To improve the quality of life and autonomy of patients; ▪ To communicate and train, promoting the sharing of knowledge and expertise in the field of rare diseases; ▪ To modernise organisations and optimise national funding mechanisms.

Implementation action(s), lead(s) and key performance indicator(s)	*Each focus will be steered by a national project leader, who will work with the relevant players to develop detailed action sheets defining the schedule for roll-out of actions and follow-up and results indicators. The actions will be delegated to a national operator where appropriate. Patient associations and healthcare professionals will be closely involved in the roll-out of actions. All the actions will be conducted in accordance with the necessary ethical principles and with a view to reducing social inequalities.* *Below focus areas and associated actions, costs, timeframes and leaders are outlined.* **<u>Focus 1: Reducing diagnostic delays and undiagnosed diseases</u>** **Action 1.1: Encourage the management of any person with or suspected of having a rare disease within a rare disease reference centre (CRMR)** Awareness-raising campaigns (in particular via the Rare Diseases Info Service (MRIS), associations, learned societies, the College of General Medicine (CMG), the bulletins of professional associations) and training initiatives for physicians will be organised so that all potential sufferers of a rare disease can be systematically referred to a rare disease competence centre (CCMR) or a rare disease reference centre (CRMR) with a view to a more rapid diagnosis. **Action 1.2: Structure genetic and non-genetic diagnostic provision** With the support of FSMRs, the French Biomedicine Agency (ABM) and Orphanet, in particular, it is necessary to: ▪ Make the organisation of and links between diagnostic technical facilities (biochemistry, haematology, pathology, foetal pathology, electrophysiology and imaging, molecular genetics laboratories, the NGS platforms of PFMG 2025) more transparent and disseminate this information to professionals and the general public ▪ Monitor and annually analyse the activities of genetics laboratories in the field of rare diseases ▪ More routinely involve molecular genetics laboratories in the work of FSMRs ▪ Assess the needs of these laboratories on the basis of scientific and technological advances in genetic diagnostic tools ▪ Specify the contribution of ERNs and their interface with FSMRs in diagnostic service provision. **Action 1.3: Define and organise access to the ultra-high-throughput sequencing platforms of the France Genomic Medicine Plan.** It is necessary to: Define and set up a mechanism for controlled access to the national platforms of PFMG 2025 for the diagnosis of rare diseases, supported by measure 6 of this plan and the implementation of multidisciplinary consultation meetings (RCPs) before and after ultra-high-throughput sequencing, directly involving the CRMRs and the molecular genetics laboratories. **Action 1.4: Establish a diagnosis observatory, supported by the clinical networks steering committee** ▪ The FSMRs will help set up this observatory, which will act on two operational levels: within the multidisciplinary committees of each FSMR and via a cross-disciplinary group dependent on the steering committee (COPIL) of the FSMRs (see Actions 10.1 and 10.2) ▪ The objective of this observatory will be to ensure the consistency of practices and the incorporation of diagnostic innovations in the management of patients, supported by scientific, technological, clinical, regulatory and ethical surveillance activities ▪ It will enable the production of annual indicators, in particular relative to diagnostic delay and undiagnosed disease evolutions in France, drawing on the national rare disease data bank (BNDMR) ▪ It will be required to interact with and be represented in PFMG 2025 bodies.

	Action 1.5: Organise and promote the systematic implementation of multidisciplinary consultation meetings The implementation of multidisciplinary consultation meetings (RCPs) helps improve the security of the diagnosis: ▪ Their composition, content and operating methods are defined by the FSMRs in consultation with the genetics laboratories ▪ Upstream and downstream RCPs will be systematically implemented in all CCMRs and CRMRs ▪ An RCP tool will be made available to CRMRs, CCMRs and FSMRs for the conduct of RCPs ▪ The arrangements for recourse to the expertise of the ERNs during multidisciplinary consultation meetings will be defined by the FSMRs. **Action 1.6: Structure foetal pathology and neonatal autopsy activities in liaison with the CRMRs and the multidisciplinary prenatal diagnosis centres (CPDPNs)** It is necessary to: ▪ Prepare an inventory of the requirements for these activities in consultation with the FSMRs and the multidisciplinary prenatal diagnosis centres (CPDPNs) ▪ Perform a review of the current organisation of these activities and assess whether the requirements are consistent with this organisation. **Action 1.7: Task the CRMRs, with the support of the FSMR, with compiling a dynamic national registry of currently undiagnosable patients on the basis of the national rare disease data bank (BNDMR)** Patient cases need to be re-assessed as knowledge and technologies advance. This will reduce the risks of loss of opportunity in terms of treatment. It is particularly important on a diagnostic level. It is necessary to: ▪ Construct an interoperable national registry drawing on data from the national rare diseases data bank (BNDMR) for people identified as "without a diagnosis" in the minimum data set ▪ Promote the implementation of research projects (see focus 5): this registry will facilitate the implementation of research projects concerning undiagnosed diseases. Wherever possible, it will be combined with biobanks that have already been compiled (identified by the FSMR) or, if applicable, with new biobanks depending on the requirements identified ▪ Task the diagnostic observatory (see action 1.4) with the production of an annual review of the data collected and the studies conducted using this registry. **Cost:** ▪ Action 1.7: Undiagnosed diseases registry: MIG (work in the public interest) funding of €3 million/year, i.e. €15M over 5 years ▪ Action 1.5: RCP tool: MIG funding of €500 K once in 2018 ▪ Action 1.1: Encourage the management of any person with or suspected of having a rare disease within a rare disease reference centre: €119 million per year, i.e. €597 million over 5 years dedicated to rare disease reference centres MSS funder for Focus 1 actions outlined above. **Timeframe:** 2018: ▪ Setting up of the diagnostic observatory ▪ Organisation of systematic upstream and downstream RCPs

	▪ Start of construction of the national registry of currently undiagnosable patients. Continuation of work to structure the provision of genetic - in liaison with the BNDMR - and non-genetic diagnostic service provision. 2019: ▪ Roll-out of the national registry of currently undiagnosable patients ▪ Structuring of foetal pathology and neonatal autopsy activities. **Leader:** ▪ Leader: General Directorate for Care Provision (DGOS) ▪ In collaboration with General Directorate for Research and Innovation (DGRI). **Focus 2: Improving neonatal screening and prenatal and preimplantation diagnostics to enable earlier diagnoses** **Action 2.1: Complete the regional and national reorganisation of neonatal screening in 2018, a necessary prerequisite to the implementation of new screening tests involving biomedical investigations.** ▪ The existing national and regional organisational structure, hinged around associations, was modified on 1 March 2018 by the establishment of a regional neonatal screening centre (CRDN) in each region, designated by the regional health agency and located in university hospital centre (CHU), and by the designation of a national coordinating centre in the second half of 2018. In their region, CRDNs will all liaise with the CRMRs responsible for the diseases screened for, within which reference doctors for the various diseases screened for will be responsible for confirmation of the diagnosis and follow-up of diagnosed infants. The aim of this revised organisation is notably to facilitate the implementation of new neonatal screening tests ▪ As regards the national neonatal screening programme for infants in French overseas regions, the majority of biomedical investigations are currently performed in mainland France, and this will remain the case. The time-frame for the implementation of the screening programme within the new organisation will be a focus of attention. **Action 2.2: Accelerate the implementation of new neonatal screening tests** ▪ Monitoring the scope of the neonatal screening (NNS) programme: in the context of the reorganisation of neonatal screening, the HAS will now be responsible for permanently monitoring NNS being trialled or considered in France or elsewhere in the world, or already implemented in another country, enabling optimal anticipation of the evaluation of new screening tests. This monitoring is currently in the process of being organised within the HAS ▪ Updating by the HAS of criteria enabling recommendation of new NNS tests**:** in 2018, the HAS has begun a methodological reflection process relative to the criteria and conduct of the assessment procedure it uses to issue opinions with respect to the implementation of a new NNS test. A comparison with the methods and criteria used on an international level will be conducted ▪ Use of genetic tests (target gene panels) in place of conventional biological tests in the context of NNS: the assessment of biological tests is part of the prior assessment of an NNS test conducted by the HAS, in collaboration with the ABM where appropriate. The use of genetic tests will be assessed by the HAS as part of its regulatory mission and within the updated methodological framework as defined. **Action 2.3: Adapt access to prenatal diagnosis (PND) to evolving technologies**

	▪ Reinforce the links between PND players: o Ensure a closer link between CPDPN consultations and CRMR consultations in the field of prenatal diagnosis (PND); o Better identify, preserve and reinforce the expertise of the players currently involved in PND (consultation of CRMRs and specialised genetics laboratories for rare diseases groups) ▪ Assess needs and adapt the resources of genetic laboratories participating in PND (in accordance with the legal framework governing PND): the growing identification - due, in particular, to NGS techniques - of genes responsible for rare diseases expands PND possibilities. "Molecular' PND is only possible if one or more pathogenic variants have first been identified, irrespective of whether an NGS or conventional method is used. In order for PND provision to develop in parallel with these discoveries, it is necessary to identify the needs (and adapt the resources) of specialised genetics laboratories for rare disease groups involved in PND so that PND implementation time-frame requirements are met for waiting couples ▪ Rules for access to France Genomic Medicine Plan platforms: Make access to PFMG 2025 platforms a priority for family sequencing requests within the context of a PND process when the use of these platforms is necessary ▪ Ethical issues related to NGS in the context of PND: identify all the ethical questions raised by the use of NGS in the context of PND in order to consider these issues as part of the preparations for revision of the bioethics law. This action is under way. **Action 2.4: Meet preimplantation genetic diagnosis (PGD) needs** ▪ Ethical issues related to NGS in the context of PGD: PGD activities are very closely regulated in terms of procedures and objectives. The issue of recourse to NGS for PGD has been raised. As part of the preparations for revision of the bioethics law, it is necessary to identify all the ethical questions raised by NGS in the context of PGD. This action is under way. In particular, concomitant testing for chromosomal defects, alongside the PGD process, which the regulations stipulate must be focused on a gene, is currently prohibited and could be discussed within the framework of this revision ▪ Evaluate the possible contribution of NGS techniques: an NGS approach could reduce the time it takes to develop a diagnostic test and hence the waiting time for each couple. Once the ethical and regulatory obstacles have been identified, pilot studies assessing the contribution of NGS in the context of PGD (reduction in development time and waiting time for couples, relative efficacy, etc.) could be envisaged. **Action 2.5: Put in place interactive electronic consent for the genetic diagnosis process** Given the development of genetic diagnosis by whole exome or whole genome sequencing for rare diseases, in conjunction with PFMG 2025, it is necessary to: ▪ Provide patients with all the information they need to give their informed consent for the genetic diagnosis process and the use of the resulting data for research purposes ▪ Better guarantee the conditions for information and informed consent, within a time interval adapted to each case, in a complex context. This implies a prior assessment of the technical, regulatory and ethical obstacles. This reflection process will be conducted in the context of the revision of bioethics laws. If the implementation conditions are feasible, consent could be linked to the patient's shared medical record (DMP), which will include a rare diseases section. These arrangements would make it possible for patients to modify their consent in the course of their care pathway, with the option of withdrawal of consent using the "blue button". **Action 2.6: Modify the legislation to allow post mortem access to genetic traits** Today, the post mortem access to an individual's genetic traits is legally authorised only if the person has previously given his/her express consent. This prevents post mortem diagnoses that could be useful in preventive terms for the family of the deceased individual. A legislative change is essential and could be envisaged within the context of the revision of the bioethics law in 2018.

	Action 2.7: Conduct a reflection process concerning screening for rare diseases in the general population, with priority given to performance of an international analysis. Screening of the general population, free from any known genetic diseases or mutations in target or non-target genes (actionable genes, i.e. those liable to mobilise preventive and/or curative measures, or even non-actionable genes) raises numerous important ethical questions, despite being technically possible today. The question is particularly relevant in the pre-conception period, primarily for the genes targeted, particularly since this type of screening is authorised in some countries for rare diseases with a significant prevalence. It is essential to begin by conducting an ethical reflection process, supported by the French national ethics committee (CCNE). Preparations for revision of the bioethics law is an ideal opportunity to launch debate concerning the issues raised. **Cost:** ▪ Action 2.1: Project to extend neonatal screening from 2019 worth €1.8 million, i.e. €7.4 million over 5 years - pending, dependent on revision of the Bioethics law and the Social Security Financing Bill (PLFSS). MSS funder for action outlined above. **Time-frame:** ▪ Finalisation of reorganisation of NNS in 2018 ▪ Structuring by the HAS of NNS monitoring activities and launch of a reflection process concerning NNS assessment criteria in 2018 ▪ Launch of a reflection process in 2018 concerning extension of the scope of NNS. **Leader:** ▪ Leader: DGS ▪ In collaboration with DGOS, DGRI, DSS, HAS, ABM, CCNE **Focus 3: Sharing data to aid diagnosis and the development of new treatments** **Action 3.1: Deployment of the BNDMR in CRMRs in conjunction with hospital information systems.** ▪ The BAMARA application based on a minimum data set for rare diseases (SDM-MR) and interoperable with hospital information systems (computerised patient record - DPI) enables the collection of named care data within CRMRs. It will be used in all rare disease centres ▪ The integration and anonymisation of data collected in BAMARA within a national rare disease warehouse that could be matched with other databases (French national health data system (SNDS), cohorts, registries etc.) This mechanism, with objectives specific to each of these two pillars, will enable strategic and medical steering of the CRMRs, provide the indicators required to monitor the plan and enable the implementation of studies that can generate new knowledge in the field of rare diseases, professional practices or the feasibility of clinical trials. **Action 3.2: Support the collection of clinical and biological data, from cohorts and registries, for their compilation, use and valuation.** ▪ France will participate via INSERM in the rare disease "implementation network" of the Go-FAIR11 initiative, which will help define interoperability standards for data warehouses on rare diseases

	▪ The development of the ORPHA nomenclature and links with other medical and disability-related terminologies will be continued by Orphanet in order to make it the reference nomenclature ▪ Warehouses of secure data that can be used for research and complying with FAIR principles will be developed within FSMRs hinged around innovative research projects. They will, therefore, be interoperable with the BNDMR, with the rare disease data warehouses of the ERNs, and with the future data platform of the EJP for Rare Diseases (EJP-RD). These projects will be selected in two phases via a call for proposals aimed at FSMRs. "FAIR Data" certification will then rapidly be sought ▪ A unit to support the assembly of data warehouses will be created, linked to the RaDiCo (Rare Disease Cohorts) programme, the platform of which meets the necessary security, quality and interoperability criteria. It will offer data warehouse coordinators methodological support for the collection of FAIR data, in liaison with the "implementation network" of the GoFair initiative mentioned above. **Action 3.3: Implementation of conditions for the reuse of data collected using e- health tools for research in the field of rare diseases** All the e-health tools used in the context of national e-health policy must be mobilised for the benefit of rare diseases, both in terms of research in this field and fair access to care (see focus 7). As regards research, this action will aim to facilitate the implementation of a dynamic electronic consent process, the secure sharing of healthcare data for research and feedback of research results to patients. Preparations for revision of the bioethics law. This action is under way. **Time-frame:** ▪ Deployment of BAMARA in all CRMRs in 2018 Implementation of the BNDMR in 2019 ▪ In 2019, selection of 5 FSMRs to lead a project for a period of 4 years ▪ In 2021, selection of a further 5 FSMRs to lead a project for a period of 4 years. **Cost:** ▪ Action 3.1: National rare disease data bank (BNDMR) €600k/year, i.e. €3 million for the period of the plan to fund the operational unit, €3 million to support the deployment of the rare disease module in the computerised data records (DPIs) as a single instalment in 2018. ▪ Action 3.2 and Action 3.3.: New FAIR data warehouses: €1.6 million per project (10 projects total i.e. 16 million over 5 years). MSS funding Action 3.1 and MESRI-PIA funding Action 3.2 and 3.3. **Leader:** ▪ DGRI and DGOS ▪ In collaboration with the DGS and the DSS. **Focus 4: Promoting access to treatments in rare diseases.** **Action 4.1: Use existing upstream assessment mechanisms more systematically in order to accelerate the registration of medicinal products and medical devices.**

	▪ Patient associations and rare disease experts could consult pharmaceutical companies to encourage the more systematic use of the HAS upstream assessment process (Early meetings, procedure for "medicinal products assumed to be innovative", fast-tracking / accelerated procedures, etc.). **Action 4.2: Create an observatory of treatments within multidisciplinary consultative assessment committees in rare disease clinical network.** ▪ To detect new substances of interest, substances to be repositioned, interesting proofs of concept, relevant off-label uses, and interesting non-medicinal approaches ▪ To identify innovative medical devices helping to improve patient care and/or follow-up ▪ To identify development or investment needs ▪ To support the development of opinions designed to advise patients and health professionals in the choice of reliable and medically relevant connected objects (a number of which can be qualified as medical devices). This action will be rolled out in close liaison with national operators (ANSM, HAS, CNAMTS, OMEDIT, ARS) but also with European operators. **Action 4.3: Manage real-life knowledge in order to reinforce knowledge of medicinal products with an MA for one or more indications in the treatment of rare diseases and set up a national organisation for the real-life follow-up medicinal products.** ▪ Promote the implementation of medico-economic studies or real-life studies to generate and collate data for all medicinal products with a marketing authorisation for the treatment of a rare disease and certain relevant medical devices. Calls for proposals such as PREPS (Performance for health systems) or PRME (Medico-economic research programme) could support studies of this type ▪ Organise data collection by CRMRs and CCMRs using a methodology enabling the follow-up of these data in real-life conditions using a disease-based method rather than drug by drug, drawing on existing databases, registries and cohorts ▪ Schedule the collection of a minimum data set by CRMRs for all off-label uses in order to elucidate practices. To this end, the minimum data set of the national data bank must be determined as soon as possible ▪ Guarantee the effectiveness of data collection implemented in the context of temporary recommendations for use (RTUs) and temporary authorisations for use (ATUs) established or issued in the treatment of rare diseases ▪ Make use of data collected by patients and families (for example, via rare disease communicating record, via expert patients, via mechanisms such as COMPILIO, etc.) ▪ For medical devices, the French national committee for the assessment of medical devices and health technologies (CNEDIMTS) may request additional studies or real-life studies in the context of its assessment of a device or a device category. **Action 4.4: Better regulate off-label prescribing practices** Proposals, to be examined in conjunction with the ANSM, the FSMRs, the CRMRs and the stakeholders within a working group, will be worked upon within the framework of PNMR3 in order to develop proposals for adaptation of the RTU system to the specificities of rare diseases. These will be based, in particular on: ▪ the organisation of a survey to be conducted by the rare diseases clinical networks (FSMRs) and the rare diseases reference centres (CRMRs) enabling the preliminary identification and prioritising of indications and medicinal products that are candidates for an RTU ▪ the establishment of dynamic off-label prescription follow-up using the rare disease module of computerised patient records (DPI)

	▪ National care and diagnosis protocols (PNDS), the development of which schedules identification of medicinal products prescribed off-label, will indicate the off-label prescriptions considered relevant by the FSMRs and the CRMRs following the abovementioned survey. PNDS must, nonetheless, indicate that the medicinal products concerned are not covered by the national health insurance system in these uses ▪ The performance of clinical trials, asking the FSMRs to mobilise available funding sources: "University Hospital Networks calls for projects (RHU of the French "Investissement Avenir" ("Investments for the future") programme), Clinical research hospital programme (PHRC12), calls for proposals for the funding of non-commercial research13. These trials will make it possible to increase the available data concerning the off-label prescribing practices given priority within each clinical network with a view to making them eligible for an RTU. **Time-frame:** 2018: ▪ Organisation of the survey to be conducted by FSMRs and the CRMRs enabling the preliminary identification and prioritising of indications and medicinal products that are candidates for an RTU. 2019: 2020: ▪ Establishment by each clinical network of applications, supported on the basis of current scientific and technical knowledge, concerning medicinal products that are candidates for an RTU, aimed at the ANSM. There will be upstream consultation between the ANSM and the clinical networks in order to best meet the requirements of the ANSM; ▪ Selection by the clinical networks of the off-label prescribing practices identified by the survey for which clinical trials would appear to be necessary in addition to the available medical and scientific data (the clinical networks will be responsible for seeking a sponsor and funding). ▪ Ramp-up of RTU examinations by the ANSM and, if applicable, of the number of clinical trials funded. **Cost:** ▪ The pharmaceutical company covers the cost of follow-up of patients treated within the context of an RTU. However, since the follow-up of medicinal products prescribed off-label without an RTU is not funded, it will be necessary to find or unblock funding sources in order to guarantee - over the period of the plan - the establishment of registries by disease by the CRMRs, which forms one of the central ambitions of this working focus; ▪ The funding sources identified will be mobilised to enable the performance of the clinical trials required to improve our knowledge of a significant number of off-label prescribing practices identified in the context of the survey conducted by the FSMRs. **Leader:** ▪ DGS and DSS ▪ In collaboration with the DGOS, ANSM, HAS. **<u>Focus 5: Giving new momentum to research in the field of rare diseases</u>** **Action 5.1 Create a research group** In particular, this group will include AVIESAN, the ANR (French National Research Agency), the FSMRs (Europe and research group), the IHU IMAGINE (university hospital network) Orphanet, RaDiCo, the FMR (French Rare Diseases Foundation) and the Ministry for Higher

	Education, Research and innovation (MESRI). Its mission will be to coordinate the participation of French players in the field of rare diseases in the activities of the EJP RD, to support the creation of consortia, via the clinical networks, for the submission of collaborative projects for European or international calls (for example IMI16 or the health programme of Horizon 2020 then Horizon Europe17 from 2021), to proactively propose ideas designed to ensure fluidity between fundamental research and clinical research in order to benefit patients, with a particular focus on the intermediate link in the chain: translational research. This group will produce an annual report analysing research activity in the field of rare diseases. **Action 5.2: Steer the construction of the EJP and coordinate the participation of French teams** ▪ The EJP RD will group together research funding activities, a data sharing and services platform, training initiatives and assistance for the transfer of research in the field of rare diseases, working closely with the ERNs. The coordinator will be INSERM. The ANR will contribute to its research funding activities. **Action 5.3: Develop human and social science-based research** ▪ The evaluation of the PNMR2 conducted by the HCERES highlighted the need to encourage cross-disciplinary collaboration in the field of human and social sciences (epidemiology, sociology, psychology, health economics, etc.). Patient associations, the FMR, the ATHENA and AVIESAN alliances and the CNSA (National Solidarity Fund for Independent Living) all have a key and complementary role to play in this action of the PNMR3, liaising closely with the CRMRs, the clinical networks, the ANSM and the HAS. A partnership needs to be developed with economists and health organisation specialists, particularly in the academic sector. **Action 5.4: Launch of a French research programme into undiagnosed rare diseases, in conjunction with the European UDNI and Solve-RD initiatives.** ▪ Undiagnosed patients are those for whom it has not been possible to reach a diagnosis based on current knowledge, including after genomic analysis. A collaborative post-genomic research programme for diagnostic and therapeutic purposes will be developed within a research network bringing together the FSMRs and fundamental research laboratories. This programme will seek to understand the mechanisms of complex or non-genetic rare diseases. This programme is similar to that of the international UDNI (Undiagnosed Disease Network International) network and the European "Solve-RD" programme, with which it will be linked. **Action 5.5: Develop mechanisms to support existing clinical research** It is necessary to: ▪ Reinforce the specialisation of certain clinical investigation centres (CICs) for rare diseases18 and explain the contribution of CICs to rare disease research with the parties involved (practitioners, patients, researchers) ▪ Publicise and reinforce the OrphanDev system, an F-CRIN-labelled platform dedicated to rare diseases hosted by Aix-Marseille University (Orphan Drug Designation, assistance with protocols, etc.) in order to expand its scope ▪ Task the F-CRIN with a support role for clinical research into rare diseases, making it easier to consult CICs, Clinical Research Units (URCs) and Clinical Research Departments (DRCs). **Action 5.6: Give priority to translational research into rare diseases** The scientific approach, which consists in starting with patients to identify genes, study their function and understand the mechanisms involved, is particularly appropriate for rare diseases. This approach requires close cooperation between clinical, genetic and pathophysiology and research teams, which share the same medical and scientific interests. Given the medical and scientific challenges, as

	well as the expertise found within CRMRs and FSMRs, it is necessary to support this translational research. To this end, translational research projects in the field of rare diseases will be given priority by the ANR and cofunded by the Ministry of Solidarity and Health (MSS) and the Ministry for Higher Education, Research and innovation (MESRI). **Time-frame:** ▪ Launch of the rare diseases research coordination group in 2018 ▪ Construction of the EJP RD in 2018 and launch in 2019 ▪ Training a group to set up an undiagnosed diseases programme in 2018 and launch of the programme in 2019. **Cost**: ▪ Action 5.4: Undiagnosed diseases programme: €4 million ▪ Action 5.2: EJP Rare Diseases: €3 million per year i.e. €15 million over 5 years. MESRI – MSS –PIA funder for above actions. **Leader:** ▪ AVIESAN ▪ In collaboration with the DGRI and the DGOS. **Focus 6: Promoting the emergence of and access to innovation.** **Action 6.1: Creation of a rare disease innovation coordination group** Led by the AVIESAN research alliance and ARIIS (Alliance for Health Industry Research and Innovation), this coordination group will bring together all rare disease innovation players (ministries of solidarity and health, higher education, research and innovation, economy and finance and ecological and inclusive transition, Athéna human and social sciences alliance, rare disease research operators and funders - including IHU Imagine and FSMRs -, patient associations, medical or paramedical professional associations, health industry unions (LEEM, FEFIS, France- biotech, SNITEM, SIDIV) and BPI France. Its mission will be to propose new innovation strategies for rare diseases and organise information sharing. It will also participate in the implementation of specific rare disease research and development mechanisms. **Action 6.2: Facilitate access to market of innovations for rare diseases** The rare disease innovation coordination group: ▪ Will identify the innovation actions already under way on a national, European and international level in the field of rare diseases, in order to optimise the work ▪ Will help update the inventory of ongoing or finalised clinical trials in conjunction with the Orphanet platform and IRDIRC ▪ Will draw up a map of innovation support mechanisms linked with the corresponding measures of the Health industries strategic council (CSIS) and the Health industries and technologies sector committee (CSF) ▪ Will formulate proposals to promote: ○ the development of new medico-economic studies for health technologies or medicinal products destined for a limited number of patients ○ the repositioning of medicinal products

	○ the development and financial sustainability of pharmaceutical-grade biotherapy bio production centres in accordance with competition regulations and the regulations governing the single European market ○ the performance of medico-economic studies or the development of real-life knowledge required by the authorities and national assessment bodies, particularly as regards academic sponsors ○ the development of therapies with proof of concept but neglected by manufacturers. **Action 6.3: Implementation of specific research and development mechanisms in the field of rare diseases** The rare disease innovation coordination group: ▪ accompany the development of rare disease projects, from proof of concept to market, supported, in particular, by SATTs (French technology transfer acceleration companies) ▪ develop a "proof of concept" club to encourage companies to take an interest in proofs of concept obtained in FSMRs or academic laboratories ▪ encourage companies, the FSMRs and French research laboratories to participate in French and European innovation programmes (FUI, PSPC, IMI etc.) ▪ raise awareness within the European Commission of the need to develop dedicated calls for proposals on the theme of rare diseases within the context of European projects ▪ create with BPI France an event dedicated to SMEs and clinical network and laboratory players, to coincide with the launch of the plan. **Time-frame** ▪ The rare disease innovation coordination group will be created in 2018 ▪ The process of identifying possible issues with respect to the emergence of innovation will take place from 2018 to 2019 ▪ Proposals for innovation transfer support and specific rare disease research and development mechanisms will be put in place in 2019. **Cost:** No additional costs. **Leader:** ▪ DGRI ▪ In collaboration with the DGS, DSS, DGE and DGOS. **<u>Focus 7: Improving care pathways.</u>** **Action 7.1: Develop information to make existing structures visible and accessible** The development of information should be based on regular, coordinated and efficient communication, not restricted to the world of rare diseases alone. Too many patients, families, care-givers and social players are unaware that resources exist to help them cope with the disease and its consequences: CRMR, FSMR, ERN, associations. Everyone should have easy access to good quality, clear information, be given relevant medical guidance or appropriate social support and know where to get help, in exactly the same way as in other areas of health. The public health information service (SPIS), Orphanet, the MRIS, associations and the FSMRs already fulfil this mission. A genuine long-term communication strategy therefore needs to be implemented, based on: ▪ Dedicated information sites, linked to general sites

	▪ A rare disease section on general information and guidance sites (SPIS, ministry websites, etc.) ▪ Regular interventions at professional conferences. **Action 7.2: Guarantee appropriate diagnosis delivery conditions** Since this is the first key moment in the care pathway, the quality of delivery of the confirmed diagnosis - or suspected diagnosis if it has not been possible to confirm it - is crucial in the management of the patient's care pathway. It is necessary to: ▪ Raise awareness and train health professionals in diagnosis delivery, offering aids to professionals developing tailored information supports for patients, their care-givers and their families ▪ Better promote the care activity of rare disease centres in line with the necessary resources ▪ Promote consultations requiring the mobilisation of several professionals (doctors, psychologists, social workers, genetic counsellors, physiotherapists, etc.) and time dedicated, and sometimes repeated, to delivery or modification of the diagnosis, follow-up in the event of an undiagnosed disease, and at pivotal moments, such as the transition from adolescence to adulthood ▪ Incorporate comorbidities in the assessment of hospital stays. **Action 7.3: Facilitate access to patient education** It is necessary to: ▪ Facilitate the dissemination of patient education programmes already authorised in a region and set up sharing tools ▪ Open up patient education sessions to multiprofessional themes ▪ Allow carers and siblings to have access to these sessions ▪ Trial online modules within patient education programmes and encourage access to these ▪ Create an information forum of existing patient education programmes (ETP), overseen by the FSMRs. **Action 7.4: Mobilise care coordination mechanisms** It is necessary to: ▪ Get general practitioners involved in their own right, via the greater use of hospital-community liaison letters ▪ Step up the production of national care and diagnosis protocols (PNDS), specific recommendations (adolescence-adulthood transition, emergency, etc.) and European guidelines applied to the French context to accompany and support good practices. This will be the subject of a specific network-based action plan ▪ Create 4 coordination platforms in French overseas territories, operating in close liaison with the CRMRs in mainland France via telemedicine ▪ Develop rare disease expertise platforms (action 10.6) in healthcare establishments housing several CRMRs ▪ Recognise and develop the care pathway coordination function in centres with territorial players ▪ Develop the broader use of emergency care support solutions (emergency medical assistance service (SAMU) information system, operational resources directory (ROR), etc.) ▪ Reinforce the regional healthcare programmes (PRS) of regional health agencies (ARS) in the field of rare diseases. **Action 7.5: Develop telemedicine and innovation in the field of e-health** It is necessary to: ▪ Make telemedicine services accessible in all Overseas reference and competence centres to enable access to mainland France reference centres and in all centres to enable access to the European expert centres of ERNs

	▪ Create an expanded patient's shared medical record (DMP) for all rare disease patients in order to ensure the portability of data and facilitate the e-pathway, which is particularly important for rare diseases. **Time-frame:** 2018: ▪ Creation of 4 Overseas coordination platforms. 2019: ▪ Definition of a service flat-rate to complete the valuation of complex, multi-professional consultations ▪ Creation of an expanded DMP for all rare disease patients. 2020-2022: ▪ Updating of all national care and diagnosis protocols (PNDS) over a 5-year period ▪ Setting-up of expertise platforms in establishments housing several CRMRs. **Cost:** ▪ Action 7.4: €400K per year for the creation of Overseas coordination platforms (€100k/year for each sector: Réunion, Guadeloupe, Martinique and French Guiana), i.e. €2 million over 5 years. €50K for a PNDS produced or updated after its 5th year, with a target of 100 PNDS each year, on a call for proposals basis. €20 million will be dedicated to this action over 5 years ▪ Action 7.3: €2 million per year for patient information on a call for proposals basis, i.e. €10 million over 5 years ▪ Action 7.1: €300K per year for the funding of Orphanet, €260K per year for the funding of MRIS, €70K per year for the funding of the Rare Diseases Alliance, i.e. a total for these 3 mechanisms of: €3.15M million over 5 years. MSS is the funder for the above actions. **Leader:** ▪ General Directorate for Care Provision (DGOS) ▪ In collaboration with the DGS and the DSS. **Focus 8: Facilitating the integration of people with rare diseases and their carers.** **Action 8.1: Facilitate access to mechanisms, rights and services dedicated to disabled people and their carers** The aim is to strengthen relationships between FSMR and MDPH players, particularly during pivotal phases in the care pathway or when the situation of rare disease patients and their carers changes. To this end, it is necessary to: ▪ Develop specific tools, on an individual FSMR or inter-network basis, for the transmission of information specific to the disability ▪ Supplement the information given to MDPH multidisciplinary teams as concerns disabilities resulting from rare diseases ▪ Improve the information supplied to FSMR concerning changes to mechanisms and the medico-social services available. **Action 8.2: Organise partnerships with the rare disabilities scheme on a national and regional level** The first and second national rare disabilities schemes resulted in the establishment of a "rare disabilities" scheme, which comprises, on a national level, a national rare disabilities coordination group and four national rare disabilities centres. On a regional level, the scheme takes the form of 12 rare disabilities relay teams (ERHR) that may be consulted by people with rare disabilities, families, associations,

	medico-social establishments, MDPHs, and care and/or welfare players. It is now necessary to: Reinforce the partnerships between players from the FSMRs and the rare disabilities scheme. **Action 8.3: Improve support processes in order to better address the needs of people with disabilities due to rare disease** It is necessary to take into account the specific needs, expectations and pathway of people with disabilities due to rare disease in conjunction with the "a guided solution for everyone" approach and the strategy for the transformation of medical and social services. **Action 8.4: Encourage the development of health autonomy support projects specific to rare diseases** The aim is to ensure the follow-up of pilot projects specific to rare diseases, undertaken in the context of the experimentation scheduled in article 92 of French law No. 2016-41 of 26 January 2016, intended to produce co-constructed assessment elements in the context of this experimentation and enable the collection of reproducible elements with a view to potential long-term application. **Action 8.5: Enable all children to have access to schooling** This action makes it possible to: ▪ Put in place the necessary schooling adaptations taking into account the health status of children with rare diseases, including for children who do not have a disability or whose disability is not recognised by the MDPH. This involves ensuring that schooling is continued in the event of repeated hospital admissions, home care or repeated treatments ▪ Improve the exchange of information between the various players in children's schooling pathways. **Action 8.6: Help people with rare diseases remain in or return employment** The aim is to ensure that rare disease patients are properly taken into account in National occupational health plan actions and manage any specificities. **Time-frame:** 2018-2022 **Cost:** No additional cost identified. **Leader:** ▪ DGCS ▪ In collaboration with DEGESCO, DGT, DGEFP, DGS and the CNSA. **<u>Focus 9: Training health and welfare professionals to better identify and manage rare diseases.</u>** **Action 9.1: Clarify the status of genetic counsellors and bioinformatics specialists and increase their training and recruitment** **For genetic counsellors**

	The "Directory of Hospital Public Service professions" recognises the profession of genetic counsellor since French law No. 2004-806 of 9 August 2004 relative to public health policy19. However, given, in particular, the low numbers of personnel trained via the degree-masters-doctorate programme in "Genetic Counselling and preventive medicine" at Aix-Marseille University (183 graduates in March 2017), there is no community of genetic counsellors, which raises issues with respect to their recruitment, remuneration and recognition. With a view to expanding the use of genetics and genomics in the management of rare disease patients, the ministries concerned, along with the French Association of Genetic Counsellors (AFCG), will conduct several studies in order to: ▪ Identify and quantify needs ▪ Undertake studies to ensure greater recognition for genetic counsellors in the clinical care network ▪ Ultimately authorise delegation to genetic counsellors of prescription of medical genetic tests ▪ Increase the training capacities of genetic counsellors and expand them to include genomic themes, with recognition within the context of continuing professional development (DPC). For bioinformatics specialists The "Directory of Hospital Public Service professions" already recognises the profession of bioinformatics specialist Although there is no established community, these professionals are recruited as senior hospital technicians and therefore have a statutory and index-related status enabling healthcare establishments to recruit them in technical and scientific fields (such as genetics and genomics, with the qualifications concerned making specific reference to bioinformatics). In view of the expansion of applied genomics applications to care and research in the field of rare diseases, it is necessary to: ▪ Identify and quantify needs. **Action 9.2: Reinforce initial training policy in medicine, pharmacy and biology programmes** The objective is to: ▪ Develop training modules on rare diseases via health simulation tools aimed at medical personnel, specialised or otherwise in rare diseases ▪ Introduce theoretical teaching modules in the field of genomics into medicine, pharmacy and biology programmes ▪ Put in place dedicated professional career paths in "Rare diseases research (Masters in biology /Health, contracts within biology / health doctoral schools and, in particular EURs (graduate research schools). **Action 9.3: Develop continuing training in the field of rare diseases** It is necessary to: ▪ Consult continuing training organisations and learned societies in order to create modules dedicated to rare diseases (classroom-based, digital, etc.) with continuing professional development (DPC) labels as incentives aimed at medical personnel ▪ Develop national DIUs (inter-university diplomas) in liaison with European DIUs including, among others, health simulation training ▪ Pool initiatives and resources on an inter-FSMR level, or even with ERNs. **Action 9.4: Encourage mixed professional/patient/family training** This involves including patients and associations in training courses for non-hospital and hospital doctors and paramedical personnel in order to raise awareness of real-life data (quality of life, etc.) among health professionals, and enable them to learn from the experience of patients, in particular via health simulation tools.

Time-frame:
2018 - 2022

Cost:
Action 9.1, Action 9.2, Action 9.3 and Action 9.4: €2 million/year, i.e. €10 million over 5 years, will be dedicated to training.
MSS will fund the above actions.

Leader:
- DGOS
- In collaboration with DGESIP.

Focus 10: Reinforcing the role of rare disease clinical networks in care and research issues.

Action 10.1: Attribute additional missions to the FSMPs over and above their current missions
- The initial missions of the FSMRs will be extended in line with the actions of the plan and will be adapted to enable individual and collective assessment
- In order to make sure that their missions have an effective and productive link with the CRMRs, a multidisciplinary consultative committee will be set up for each clinical network.

Action 10.2: Structure the FSMR steering committee
The existing clinical network steering committee will evolve:
- Its meetings will be jointly organised by the Ministry of Solidarity and Health (MSS) and the Ministry for Higher Education, Research and innovation (MESRI)
- Patient associations, along with national rare disease players such as Orphanet, MRIS, RadiCo, the FMR and IHU Imagine will be regularly invited
- Inter-network exchange will be fed by the work of themed groups (Diagnostics, Therapies, Databases and Biobanks, Research, Europe, Care pathways, Training) in close liaison with clinical network multidisciplinary consultative committees.

Action 10.3: Ensure assessment of FSMPs and their CRMRs
A monitoring committee for labelled CRMRs and FSMRs will be appointed and will
- Ensure the durability and structuring of labelled centres and clinical networks
- Analyse specific situations arising during the mandate
- Assess the performance of these structures in line with their activities and missions
- Make proposals for the revision of activity indicators and the distribution of available funds
- Propose medium or long-term changes regarding their scopes.

Action 10.4: Renewal of FSMRs
Since the mandate of the FSMRs ends in 2018, following an assessment of the scope of the FSMRs and their coherence with the ERNs, a new FSMR designation process will be carried out in 2018, via projects incorporating healthcare, medico-social, research and innovation and training aspects, submitted by candidate network leaders.

	Action 10.5: Consolidate the operational resources of FSMRs. In order to ensure that their operational resources evolve in line with the implementation of their missions: ▪ A Ministry of Solidarity and Health/FSMR/Establishment housing the FSMR/competent Regional Health Agency agreement will clarify the conditions for the allocation of basic funding for their operation (excluding specific calls for proposals) ▪ Basic rules of procedure specifying full members (research team representative, association representative, etc.) and the missions will be adapted for each FSMR, containing paragraphs specific to their field ▪ Consortium agreements could be put in place in order to clarify the distribution of funds, intellectual ownership rules, a single authorised representative, etc. **Action 10.6: Encourage healthcare establishments to set up rare disease expertise platforms to strengthen inter-network links within the host establishments of several labelled centres.** Rare disease expert platforms group together- within the same university hospital group, group of healthcare establishments or regional hospital grouping - reference centres that organise the care network for different rare diseases, diagnostic laboratories and research units, as well as the patient associations concerned. The aim of these platforms is to share expertise and pool knowledge and skills on a local level in order to: ▪ Raise the profile of labelled rare disease centres ▪ Support diagnostic and therapeutic innovation and research ▪ Reinforce links between centres and patient associations ▪ Promote the implementation of rare disease databases ▪ Facilitate medico-social actions in centres. Rare diseases expertise platforms are not intended to replace existing structures, such as competence centres or national clinical networks. On the contrary, their purpose is to help health establishments work more effectively together. **Time-frame:** 2018: ▪ Appointment of the CRMR and FSMR labelling monitoring committee ▪ Ratification of multipartite agreements on FSMR resources. ▪ Call for proposals concerning the renewal of FSMRs 2019: ▪ Establishment or revision of rules of procedure ▪ Implementation of the clinical network multidisciplinary committee. **Cost:** ▪ Action 10.1: €119 million/year, i.e. €597 million over 5 years for the CRMRs, €12.7 million/year, i.e. €63.5 million over 5 years for the FSMRs ▪ Action 10.6: €200K/year for the initiation, on a call for proposals basis, of expertise platforms within healthcare establishments or hospital groupings hosting several CRMRs, i.e. €8 million over 5 years, for 40 platforms (call for proposals for 10 establishments in 2018, 2019, 2020, 2021).

	MSS will fund the above actions. **Leader:** ▪ General Directorate for Care Provision (DGOS) ▪ In collaboration with General Directorate for Research and Innovation (DGRI). **Focus 11: Specifying the positioning and missions of other national players in the field of rare diseases.** **Action 11.1: Maintain and amplify the contribution of patient associations and relatives' associations in the definition and implementation of rare disease policy** ▪ Increase their participation in steering bodies and at all levels in the operational implementation of this policy, particularly in the steering committee of FSMRs ▪ Identify innovative experiences and practices in terms of the participation of patients and their increased autonomy in order to further improve the roll-out of health democracy ▪ Train patient associations in adapted clinical trial methodologies (questionnaires, surveys, database use, etc.) and ethical issues, via training courses leading to qualifications. **Action 11.2: Reinforce the role of PORHANET and ensure its long-term funding** ▪ Information concerning the resources and organisation of the care pathway in France will be supplemented to better address the information needs (emergency situations, related disabilities, information documents for patients) of all the field's players ▪ Orphanet will continue its actions in the area of the production, updating and dissemination of ORPHA nomenclature, necessary for the interoperability and reuse of rare disease data in France and Europe ▪ A reflection process on the financial sustainability and status of Orphanet, launched within the framework of the joint RD-Action, will be completed. **Action 11.3: Encourage the Rare Diseases Foundation (FMR) with research alliances** The role of the FMR is particularly well known in the field of human and social sciences, animal models, treatment screening and genomics projects. Whilst it must maintain its status and funding sources, it must nonetheless be better integrated into the dynamics of the actions proposed for rare diseases. The following is proposed: ▪ A more integrated relationship with the AVIESAN Alliance, with the scientific collaboration of the FMR in the Genetics Genomics Bioinformatics (GBB) Multi-organisation themed institute (ITMO) without compromising the operation of the Foundation and its missions ▪ To include representatives from the AVIESAN and ATHENA alliances in the FMR's Scientific Board. **Action 11.4: Reinforce the role of the RaDiCo in the integration of research data for rare diseases** The support unit for structuring of data used by RaDiCo will be enhanced: ▪ establishing operational links with the National rare disease data bank (BNDMR) ▪ proposing technical and ethico-regulatory support for the creation by the FSMRs of new interoperable data warehouses, and studying the possibility of hosting these new warehouses on the RaDiCo platform ▪ establishing operational links with the data platform of the EJP RD and the databases of the European Reference Networks that are in the process of being assembled.

	Time-frame: 2018: ▪ Closer collaboration between the FMR and the Aviesan alliance, 2018-2019; ▪ Reinforcement of the role of RaDiCo in the integration of research data for rare diseases. 2019: - Proposal of methods to ensure the sustainability of Orphanet **Cost:** See action 7.1 **Leader:** ▪ DGS, DGOS and DGRI ▪ In collaboration with AVIESAN.
Governance and organisational structures	**Each focus will be steered by a national project leader, who will work with the relevant players to develop detailed action sheets defining the schedule for roll-out of actions and follow-up and results indicators. The actions will be delegated to a national operator where appropriate. Patient associations and healthcare professionals will be closely involved in the roll-out of actions. All the actions will be conducted in accordance with the necessary ethical principles and with a view to reducing social inequalities.** **The Strategic Committee** ensures application of the plan by mobilising partners and resources. It guides its implementation and proposes adjustments to the plan on the basis of the evolving context. It validates the annual report proposed by the operational committee that it submits to the Prime Minister. It is chaired by the cabinets of the Ministry of Solidarity and Health and the Ministry of Higher Education, Research and Innovation. It is composed of: ▪ the central departments of these two ministries: DGOS, DGS, DGCS, SGMAS, DGRI, DGESIP ▪ representatives of the Ministries for the Economy and Overseas and of the secretariat of State for Disabled People ▪ two representatives from the rare disease clinical networks; ▪ a representative of the National Association of Molecular Genetics Practitioners (ANPGM) ▪ the project leader of the France Genomic Medicine 2025 plan ▪ the President of Aviesan ▪ representatives of patient associations: French Myopathy Association (AFM), Rare Diseases Alliance, Eurordis, Vaincre la mucoviscidose (VLM - cystic fibrosis association), French Haemophiliacs Association (AFH) ▪ the presidency of the HAS ▪ a representative from general directors of the regional health agencies ▪ a qualified person having coordinated the drafting of the report on PNMR3: S. Odent ▪ the chair and vice-chair of the operational committee (see below) ▪ a representative of the LEEM and a representative of SNITEM.

	It meets at least once a year. **The Operational Committee** is responsible for implementing the actions of the Plan and reporting back to the Strategic Committee. It ensures actions are implemented in accordance with the scheduled calendar, assesses the results of the Plan using indicators and monitors spending compared to the scheduled budget. It prepares the annual report for the Plan. The operational committee is chaired by two personalities appointed by the Ministry of Solidarity and Health (MSS) and the Ministry for Higher Education, Research and innovation (MESRI) (chair and vice-chair), who are assisted by the rare diseases mission, composed of MSS and MESRI members and the secretariat of which is handled by the General Directorate for Care Provision (DGOS). It is composed of: ▪ representatives from the DGOS, DGS, DGCS, DGRI and DSS and AVIESAN, piloting the 11 focuses ▪ representatives of the agencies and operators involved in the plan's actions: ABM, HAS, ANSM, ANSP, CNSA, AVIESAN, Orphanet, FMR ▪ representatives of three patient associations ▪ representatives of two rare disease clinical networks ▪ the president of the CRMR and FSMR labelling monitoring committee. It meets at least once a year.
Funding model	*Costs of each Focus Area and funding bodies for these costs are outlined (see implementation actions).*
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	*See Action 2.1 , 2.2, 2.3, 2.7*
Personalised medicine, genomics, genetic counselling	*See Action 1.2, 1.3, 2.4, 2.5, 2.6*
Models of care/care pathways	*See Action 7.1, 7.2, 7.3*
Workforce	*See Action 9.1, 9.2, 9.3, 9.4*
European Reference Networks	The 23 rare disease clinical networks (FSMRs) are linked to the 20 European Reference Networks for rare diseases (ERNs) created in 2017, in terms of themes and missions. One of the current missions of each clinical network with respect to a group of diseases enable:

	▪ Pooling of resources and expertise on a national level in order to raise visibility on an international level, in particular via European reference networks. *See Action 11.4- "establishing operational links with the data platform of the EJ RD and the databases of the European Reference Networks that are in the process of being assembled."*
EU alignment and participation	*See Action 6.2* *See Action 6.3- "raise awareness within the European Commission of the need to develop dedicated calls for projects".* *See Action 7.4- "Step up the production of national care and diagnosis protocols (PNDS), specific recommendations (adolescence-adulthood transition, emergency, etc.) and European guidelines applied to the French context to accompany and support good practices. This will be the subject of a specific network-based action plan"* On an international level, the strategy incorporates international challenges in the area of rare diseases, such as the new objectives of the International Rare Diseases Research Consortium (IRDiRC), the European Reference Network (ERN) structure and the future European research programme for rare diseases (European Joint Programme/EJP).
Health information (including rare disease registries)	*See Action 1.7, 3.1, 3.2*
Orphan medicines	*See Action 4.1, 4.2, 4.3, 4.4*
Rare disease research	*See Action 3.3, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6*
Alignment beyond the healthcare sector	*See Action 6.1, 11.1, 11.3*
Any additional information (for example, background to the strategy or strategy development)	This plan is the third rare disease plan in France. The first two plans contributed to some major advances. They boosted national excellence - in both treatments and research - and helped France become a European leader. However, this position needs to be further reinforced. Competence centres, reference centres and clinical networks now form the basis of an organisational structure ensuring access to care and expertise for all. The first plan encouraged patient associations and healthcare players to liaise more closely. The drafting of this plan was coordinated by two qualified persons: Professor Yves Levy, President of Aviesan (French national alliance for life sciences and health), and Professor Sylvie Odent, a professor of medical genetics and manager of a rare disease reference centre. Nonetheless, the organisation of healthcare for these patients continues to pose some specific problems, related to access to a diagnosis, with a diagnostic delay that remains excessively long, requiring continued efforts in terms of structuring and coordination. These diseases also pose a number of specific research challenges. Given their rarity, they require the creation of national databases, which must be able to interact with European databases. These tools will make it possible to speed up the development of knowledge and the assessment of new care strategies and new treatments. Lastly, research into rare diseases falls within the general scope of the growing role of genomics in the elucidation of the molecular mechanisms of diseases and, consequently, the challenges go beyond the actual diseases themselves.

	Main quantitative objective of PNMR3: In line with the IRDiRC3 consortium, this plan aims to ensure all people living with a rare disease receive an accurate diagnosis, care and available therapy within one year of their first specialised medical consultation. The only patients without an accurate diagnosis one year after their first consultation with a specialist are limited to those for whom current scientific and technical knowledge does not enable an accurate diagnosis made. This plan also aims to ensure that all currently diagnosable patients enter a globally coordinated diagnostic and research pipeline. **Developing the strategy** As with the previous two plans, the method chosen brought together all the relevant stakeholders from the community, patient associations, Ministries, state agencies, health and research professionals and industry players, and care was taken to ensure the plan is in line with European Commission initiatives. This huge collective task involved more than 160 people, working together to construct the plan, the name of which encapsulates its considerable ambitions: "Sharing innovation: a diagnosis and treatment for all".

Note: See abbreviation list in Themes or Priorities section.

Table B13. Data extracted for Germany (NAMSE main strategy)

Germany	Strategy information
Author(s) **Title**	National Action League for People with Rare Diseases (NAMSE) National Plan of Action for People with Rare Disease: Action Fields, Recommendations, Proposed Actions[32]
Timeline	Established in 2013 (no end date).
Overall aim(s)	The National Action Plan has two main goals: to prepare policy suggestions and proposed actions. It then names a number of action fields (see Themes and or priorities) and a number of goals associated with each.
Themes and or priorities	**Action Field 1: Care, centres, networks** ***Areas:*** ▪ The Center Model for Rare Diseases ▪ Orphan Drugs, Off-Label Use and Evidence Generation. ***Goals:*** ▪ Define the various steps to be taken by the centres and networks and prepare their implementation ▪ Define the range of tasks and methods to be employed by the centres and networks as well as the criteria for identifying and designating these organizations ▪ Develop suggestions for the long-term funding of such centres and networks ▪ Optimize the supply of both approved medicines and off-label-use medicines. **Action Field 2: Research** ***Areas:*** ▪ Etiology and Genome Analysis ▪ Pathophysiology and Disease Mechanisms ▪ Development of Diagnostic Test Systems ▪ Investigator-Initiated Trials: Prospective, Controlled Clinical Studies ▪ Health Services Research ▪ Ethical, Legal and Social Aspects ▪ Cooperation Between Academia and Industry ▪ Cooperation with International Partners ▪ Establishing Centers for Rare Diseases. ***Goals:*** ▪ Improve the overall conditions for research and development in the area of rare diseases ▪ Accelerate the transfer of research knowledge to practical applications ▪ Improve research on optimizing therapy ▪ Improve health services research.

	Action Field 3: Diagnostics ***Areas:*** ▪ Initial Contact: Primary Care ▪ Diagnostic Software Technologies ▪ Innovative Sequencing Technologies for Molecular Diagnostics ▪ Guidelines. ***Goals:*** ▪ Accelerate the diagnostics of rare diseases ▪ Develop strategies for dealing with an unclear diagnosis ▪ Improve the design of guidelines. **Action Field 4: Information Management** ***Areas:*** ▪ Adequate Patient Information on Rare Diseases ▪ Joint Communications on the Subject of Rare Diseases ▪ Central Information Portal ▪ Medical and Dental Training and Continued Education ▪ Public Relations ▪ Telemedicine. ***Goals:*** ▪ Increase awareness for rare diseases in both the general public and among experts ▪ Improve the level of information available to and information procurement by those afflicted, ▪ their relatives, doctors, therapists and caretakers ▪ Improve the training and further education of medical, therapeutic and caretaking personnel. **Action Field 5: Implementation and Future Development** **Cross-sectional Action Field: Patient Orientation** Additionally the cross-sectional action "patient organizations to improve the medical treatment situation of persons with rare diseases" should be across all action fields and goals. In this scheme, representatives of the various patient organizations introduce the knowledge they have gained, through a regular exchange of ideas and opinions with affected persons, into the various committees that play a role in the healthcare system, in particular in those of the Federal Joint Committee. The joint aim of all involved is the improvement of patient orientation throughout the healthcare system. Patient organizations are particularly welcome in situations in which there are deficits in the existing care or where research in rare diseases is lacking. To be effective, patient advocacy requires a framework that provides sufficient support. ***Areas:***

	▪ Research ▪ Expert Opinions by the Medical Advisory Service of the German Statutory Health Insurance ▪ Support and Qualification of Patient Organizations ▪ European Networks. **Cross-sectional Action Field:** Registries ***Areas:*** ▪ Web-Portal of Registries of Rare Diseases in Germany ▪ Steering Committee of Registry Operators for Exchanging Information on "Registries on Rare Diseases" ▪ Development of Software for Establishing a Databank Prototype to Implement and Manage a Disease-Specific Registry for Rare Diseases ▪ Registry of "Patients with an Unclear Diagnosis" ▪ Project "Non-Disease-Specific Registry".
Targets (if specified) and measurement method(s) (where available)	*A number of Goals are listed for each action field however targets are not provided.*
Implementation action(s), lead(s) and key performance indicator(s)	(Description not extracted for each action field) **<u>Action Field 1: Care, centres, networks</u>** ***Area:*** ▪ The Center Model for Rare Diseases. ***Recommendation:*** NAMSE recommends the establishment of centres for rare diseases at three different, cross-linked levels of specialization. These levels are not to differ in the quality of the care they provide, but only in the spectrum of services they offer. They are to be embedded in the local healthcare structures in both primary and specialist care. The three levels of specialization in the model of cross-linked centres for rare diseases are to be differentiated according to whether the treatment they offer is outpatient/inpatient or disease (group) specific/non-disease specific. - The type C centres (cooperating centres for a specific rare disease/disease group x) are to be responsible for disease-specific or disease-group specific, interdisciplinary and multi professional outpatient care. A type C center (cooperating center) is to be primarily concerned with delivering concrete care for patients with a confirmed diagnosis or a clear suspected diagnosis. Type C centres may include non-hospital subspecialized practices, group practices, medical care centres or hospitals. - Type B centres (centres of expertise for a specific rare disease or disease group x) are also to be organized around certain specific rare diseases or rare disease groups for patients with a confirmed diagnosis or a clear suspected diagnosis. However, they are to offer not only outpatient but also inpatient, interdisciplinary and multi professional care. Thus, the type B center (center of expertise) is to be an established hospital that is equipped to deal with a specific rare disease or rare disease group both on an inpatient and an outpatient basis. - Type A centres (reference centres for rare diseases, with centres of expertise for xyz) are to consist of more than two type B centres (centres of expertise) and offer, in addition, special non-disease specific structures (for example, for the treatment of patients with unclear diagnoses, patient guides, interdisciplinary case conferences, innovative special diagnostics). Type A centres (reference centres) are to be

	the referral centre for patients with an unclear diagnosis; they are also to do basic and clinical research and they are entitled to provide training tools and training sessions covering the medical dimension of care for undergraduate medical students at medical school. The individual non-disease specific interdisciplinary tasks of the type A centres (reference centres) are to be as follows: ▪ To guide patients with specific diagnostic or therapeutic needs to their proper place within the system (seamless patient pathway and, if necessary, national and Europe-wide routing). ▪ To provide standardized methods of diagnosis for patients with an unclear diagnosis who demonstrate a high probability of having a rare disease. Type A centres also participate in remote diagnostic procedures (for example, , telemedicine, teleconsultation, symposia to review unclear diagnoses and standard operating procedures between the centres; the latter are especially important with respect to the role of the European reference networks). ▪ To provide comprehensive resources that can be used centrally for multiple medical facilities and multiple rare diseases, such as patient registries, biobanks, innovative special diagnostics, etc. ▪ To offer a range of continuing medical education courses for the specific rare diseases in cooperation with the patient organizations. ▪ To participate in the European reference networks for rare diseases in accordance with the provisions of Directive 2011/24/EU of the European Parliament and the European Council. ▪ Together with the type B centres (centres of expertise), to develop uniform recommendations for the diagnosis and therapy of rare diseases, which are regularly updated in accordance with the newest scientific evidence. These recommendations are then to form the basis for patient care at all three levels (types A, B and C). ▪ Together with type B centres (centres of expertise), to support the work of the type C centres (cooperating centres) with special diagnostics and procedures for confirming diagnoses. ▪ To provide a multidisciplinary research infrastructure where both basic and clinical research as well as research into healthcare provision can be carried out. Because of the large number of rare diseases, no single type A centre (reference centre) will be able to cover the entire spectrum of possible diseases. So as to be able to cover as many rare diseases as possible, a national network of type A centres (reference centres) is necessary to provide a coordinated effort for the diagnosis of unclear cases, to conduct training, continuing and further medical education and to develop quality standards for documentation. Further, type A centres (reference centres) should be cross-linked to all type B centres (centres of expertise) and type C centres (cooperating centres). They could provide support for activities such as patient documentation (registries), diagnosis confirmation, counselling and consultancy, and compliance with the newest therapy recommendations and integrate the type B centres (centres of expertise) and the type C centres (cooperating centres) in research activities, in particular in clinical studies and health services research. To this end they are to provide the necessary infrastructure (for example, software). A preliminary list of the criteria to be met can be found in Appendix 2 to this publication. Of course, this list is not final and needs to be further developed, concretized and operationalized in order to serve as a basis for any future designation process. Any facility seeking to belong to one of the three levels of care described above will have to provide proof that it fulfils the criteria listed in the then finalized list of criteria. This assumes the development of a transparent and replicable method of designating the three different types of rare disease centres. Such proof of competence will serve as a signal to both providers and patients that the institution has been designated based on objective criteria. It can be assumed that, in the first phase, the designation will be based on a self-declaration by the applicant centre, which the NAMSE Coordinating Office will examine for completeness and plausibility based on the documents submitted along with the self-declaration. In the beginning, no further examination, such as on-site inspections or the review of the fulfilment of criteria, is foreseen.

	However, a proper designation body will have to be created as soon as possible to ensure compliance with the criteria. The structures for the certification of cancer centres in Germany may serve as a model in developing this designation body. The designation awarded by this body is to be valid for 3 years. NAMSE has already described the existing possibilities for funding outpatient care structures in the German healthcare system. Funding options were outlined for all three types of centres within the existing legal framework. The following were discussed in detail with respect to their suitability for funding the three types of centres of expertise: (1) Highly specialized outpatient care (§116b Social Code Book V), (2) care by panel doctors and dentists (§§95ff Social Code Book V) including care provided by hospital physicians or clinics authorized to provide outpatient care (§§116, 116a Social Code Book V), (3) enabling provisions for university outpatient clinics (§117 and 120 Social Code Book V) as well as social-paediatric centres (§119 Social Code Book V). In addition, besides the collective agreements, there are the selectively contracted conditions for remunerating special services within the framework of integrated care (§§140a ff Social Code Book V) or specialized medical care (§73c). However, selectively contracted solutions have proven to be unsuitable for ensuring universal access to care for the small numbers of persons affected because of the specific challenges faced in the area of rare diseases. Instead, the existing funding possibilities offered by collective contracts are to be used to finance the systematic implementation of the three-tiered structure of centres for rare diseases. The NAMSE partners will urge that the necessary funds that are not already included in the existing standard remunerations be made available by the payers. ***Proposed action 1:*** Existing funding options are to be used to ensure funding for the three-tiered structure of the centres for rare diseases. Special healthcare services for treating persons with rare diseases, in particular type A centres (reference centres), are to be taken into account within the framework of the negotiations for the remuneration of inpatient and outpatient care. In an advisory capacity, representatives of patient interests will work together with representatives of both the healthcare providers and the third-party payers to clarify the common criteria and requirements for funding the centres. They shall work together to ensure that the third-party payers can agree locally to provide the funds not already included in the existing standard remunerations. Once questions of funding and implementation have been resolved, it is recommended that the care providers implement the three-tiered model of "CenAction Field: Care, Centers, Network Centers for Rare Diseases (A, B, C)" in accordance with the suggested definition, taking into account the agreed preliminary list of the criteria to be met). **Implementation:** short-term (1 to 2 years) **Responsible bodies:** German Hospital Federation (DKG), Association of University Clinics in Germany (VUD), Federal Association of Statutory Health Insurance Funds (GKV-Spitzenverband), healthcare providers. ***Proposed action 2:*** Suitable healthcare providers desiring to be designated as centres of expertise for rare diseases type A (reference centre), type B (centre of expertise) or type C (cooperating centre) according to the proposed definition of the NAMSE three-tiered model of centres for rare diseases and taking into account the commonly agreed upon criteria, should make this known to the NAMSE Coordinating Office. In the course of a transparent preliminary procedure that must be equally accepted by all parties involved, including the patient representatives, the NAMSE Coordinating Office will examine the declaration of intent, substantiated by the evidence submitted, to determine completeness and plausibility. A central designating body analogous to that found in the certification procedure for the German cancer centres should be set up as quickly as possible. The designating body will issue designations valid for 3 years. In this entire process, the establishment of standards, the inspection of conformity to these standards, designation by an appropriate coordinating office, as well as an independent committee structure should be kept as separate from one another as possible. The designated centres of expertise are to be listed in an overview on the homepage of the coordinating office with reference linking for both providers and patients.

	Implementation: short-term (1 to 2 years) **Responsible bodies:** NAMSE partners (see additional information) ***Proposed action 3:*** Two years after the implementation of the National Action Plan, the German Federal Ministry of Health (BMG) shall, together with the other NAMSE partners, evaluate the designation process and determine whether the funding elements contained in the existing standard remunerations are sufficient to fund the centres of expertise or whether new legislation is necessary. **Implementation:** medium-term (3 to 5 years) **Responsible bodies:** BMG, NAMSE partners. ***Area:*** ▪ Orphan Drugs, Off-Label Use and Evidence Generation ***Recommendation:*** NAMSE supports guaranteeing and optimizing the quality-assured treatment of patients with authorized medications for rare diseases, including the local care of patients in everyday life. It must be ensured that, following initial prescribing and regular monitoring of the treatment at a centre of expertise, follow-up prescribing by office-based panel doctors (non-hospital physicians) or local hospitals should be possible. In order to improve the availability of medicinal products for rare diseases and to provide evidence supporting this use, NAMSE further recommends the generation of the necessary data documenting the extent of off-label use of medicinal products for rare diseases. ***Proposed action 4:*** Given the problematic situation with orphan drugs (financing, interruptions in care), efforts are being made to determine whether further measures for procuring medicinal products for persons with rare diseases are still necessary once the centre model for rare diseases has been implemented. **Implementation:** medium-term (3 to 5 years) (once the centre has been established) **Responsible bodies:** BMG, the self-administration structure, type A centres (reference centres), type B centres (centres of expertise) or type C centres (cooperating centres). ***Proposed action 5:*** Within the framework of a health services research study based on the available data, a first step will seek to describe the care of patients with rare diseases using orphan drugs during inpatient care in a hospital as well as during inpatient rehabilitation, regardless of whether or not this inpatient care was due to a rare disease. In the process, special attention should be given to the potential problems with the funding of orphan drugs, as well as the approach taken hitherto with the problems encountered. On this basis, the need for supplementary measures should also be investigated. **Implementation:** Short-term (1 to 2 years) **Responsible bodies:** GKV-Spitzenverband, DKG, BMG. ***Proposed action 6:*** An expert opinion is to be commissioned to examine the possibilities of gleaning knowledge from the routine provision of patients with authorized medicinal products and the off-label use of medicinal products. This should include investigating in advance which data from routine use can be put to good use. Worthy of consideration would be data from healthcare providers, which are gathered as part of the statutory obligation to document treatment, as well as data transmitted to the statutory insurance funds in the course of the invoicing process. In the latter case, use can be made of the data that are transmitted by the Federal Office of

	Administration, in compliance with the Ordinance on Data Transparency, to the German Institute for Medical Documentation and Information (DIMDI), which places them in anonymous form at the disposal of specific user circles. However, these data are not likely to be available before the end of 2013. The expert opinion in question should, in particular, address the question of which of the data that are currently being collected can be used for this purpose, how data collection can be expanded and, if necessary, medical documentation standardized in such a way as to generate such information from the day-to-day provision of medical care. In addition, the usefulness of this additional knowledge (for example, in generating new hypotheses or controlling the flow of patient care) should be weighed against the necessary expenses. Note that this shall be without prejudice to the evidence hierarchy established by the Federal Joint Committee of Physicians and Health Insurance Funds (G-BA). **Implementation:** Short-term (1 to 2 years) **Responsible bodies:** BMG (German Federal Ministry of Health). ***Proposed action 7:*** (a) A study to determine the extent of off-label drug use in rare diseases, based on the data gathered pursuant to §303a ff Social Code V (SGB V) in conjunction with the Ordinance on Data Transparency of the German Federal Ministry of Health of 10 September 2012, to be carried out by one of the institutions empowered pursuant to § 303e sub-sect. 1. (b) Ranking of rare diseases according to their in terms of treatment with off-label drug use, based on the data gathered pursuant to §303a ff Social Code V (SGB V) in conjunction with the Data Transparency Act of the German Federal Ministry of Health of 10 September 2012, to be carried out by one of the research institutions empowered to do so. (c) Evaluation of the results pursuant to Chapter 4 of the Rules of Procedure of the G-BA and, where applicable, commissioning by the G-BA of the expert commissions according to § 35c sub-sect. 1 Social Code V (SGB V) to determine the status of the existing scientific knowledge. If necessary, additional expert commissions according to § 35c sub-sect. 1 SGB V may have to be set up. (d) Establish the infrastructure for clinical trials with medicinal products approved for human use that could be carried out at clinical trial centres specializing in rare diseases, particularly with respect to off-label use. **Implementation:** Short (1 to 2 years) and long-term (over 5 years) (once the centre has been established) **Responsible bodies:** BMG, type A centres (reference centres), type B centres (centres of expertise), type C centres (cooperating centres), G-BA, pharmaceutical companies. **<u>Action Field 2: Research</u>** ***Area:*** ▪ Etiology and Genome Analysis ***Recommendation:*** NAMSE recommends that selected sequencing centres for rare diseases be established or supported, primarily in type A centres (reference centres). These sequencing centres should pursue the following tasks: a) Do research into the genetic causes of previously unresolved rare diseases in order to improve their diagnostics b) Join in national and international networks of clinical workgroups and coordinate the collection and preparation of biological material to resolve the question of phenotypes c) Do research into and improve the techniques for using next generation sequencing (NGS) data in this context d) Consolidate national and international databases on NGS diagnostics and phenotyping

	e) Do research on and instigate discussions surrounding the medical-ethical conditions for carrying out research projects that involve genome information. ***Proposed action 8:*** Set up and expand sequencing centres for rare diseases. **Implementation:** short-term (1 to 2 years) (once the centre has been established) **Responsible bodies**: German Federal Ministry for Education and Research (BMBF), type A centres (references centres), type B centres (centres of expertise) or type C centres (cooperating centres). ***Area:*** ▪ Pathophysiology and Disease Mechanisms ***Proposed action 9:*** Support research projects on rare diseases that comprise the use of animal or cell models to elucidate the pathophysiology of rare diseases. **Implementation:** short-term (1 to 2 years) **Responsible bodies:** BMBF, German Research Foundation (DFG), other research sponsors. ***Area:*** ▪ Development of Diagnostic Test Systems ***Proposed action 10:*** Intensify research to develop diagnostic procedures for rare diseases. **Implementation:** short-term (1 to 2 years) **Responsible bodies:** BMBF, DFG, other research sponsors, diagnostics industry. ***Area:*** ▪ Investigator-Initiated Trials: Prospective, Controlled Clinical Studies ***Proposed action 11:*** Specialization of clinical research units dedicated to the study of rare diseases. **Implementation:** short-term (1 to 2 years) (once the centre has been established) **Responsible bodies:** Type A centres (reference centres), BMBF. ***Area:*** ▪ Health Services Research ***Proposed action 12a:*** Induce a multidisciplinary discussion on the state of health services research in order to take stock of and identify gaps in the research on the care of rare diseases as well as possible solutions. **Implementation:** short-term (1 to 2 years) (once the centre structure has been established) **Responsible bodies:** BMBF, BMG, ACHSE e.V.

	Proposed action 12b: Based on the results of the above-mentioned multidisciplinary discussion, support the set up and expansion of the appropriate scientific personnel base in the field of health sciences research in rare diseases through the establishment and integration of such research in the centres for rare diseases. **Implementation:** short-term (1 to 2 years) (once the centre structure has been established) **Responsible bodies:** Type A centres (reference centres), type B centres (centres of expertise) or type C centres (cooperating centres), BMBF. ***Area:*** ▪ Ethical, Legal and Social Aspects ***Recommendation:*** Because of the increasing demands being made on research into the ethical, legal and social aspects (ELSA) of modern life sciences and biotechnology, the BMBF has funded ELSA research since 1997. The focus of ELSA is part of the Framework Program of the German Federal Government on health research. This program addresses questions concerning political and societal dimensions as well as medical ethics. NAMSE thus recommends continuing this path and including the viewpoint on rare diseases. As a further focal point. ***Proposed action 13:*** Continuation of the ELSA funding program. **Implementation:** short-term (1 to 2 years) (once the centre structure has been established) **Responsible bodies:** BMBF. ***Area:*** ▪ Cooperation Between Academia and Industry ***Proposed action 14:*** Implementation of a cooperative platform to broker the engagement between academia and industry. This should include patient organizations as well as small and medium-sized companies as part of a multistakeholder process. **Implementation:** short-term (1 to 2 years) (once the centre structure has been established) **Responsible bodies:** NAMSE coordinating office, BMBF, industrial partners (German Association of Research-based Pharmaceutical Companies and Federal Association of the German Pharmaceutical Industry), academic partners including type A centres (reference centres), type B centres (centres of expertise) or type C centre (cooperating centres), research associations of rare diseases. ***Area:*** ▪ Cooperation with International Partners ***Recommendation:*** The BMBF is participating in the ERA-Net Initiative "E-Rare" since 2003. This organization has the goal of coordinating research funders in the European Union (EU) and EU-associated countries. A continuation through 2014, E-Rare-2, is also in place. This cooperation serves to collect information about research going on into rare diseases in these countries, to strategically coordinate these activities and to fund transnational research projects. Rare diseases are a key priority in the 7th Framework Program (2007-2013) of the European Commission. In the first four calls for proposal in the years 2007 through 2010 some 50 joint projects were funded with over EUR 237 million; ca. EUR 100 million were foreseen for further projects in the 2011 call. In addition, together with the US National Institutes of

	Health, the EU Commission founded the Rare Diseases Research Consortium in 2010, the goal of which is to develop 200 new therapies and diagnostic procedures for most rare diseases. NAMSE recommends supporting and continuing the initiatives mentioned above. ***Proposed action 15:*** Continued strategic development of research funding of international cooperation in the field of rare diseases. **Implementation:** short-term (1 to 2 years) **Responsible bodies:** BMBF, DFG, other research sponsors. ***Area:*** ▪ Establishing Centers for Rare Diseases ***Proposed action 16:*** Provide support for innovative concepts to connect the patient care and research at the individual locations in order to enable a close cooperation between fundamental research on the one hand and clinical research on the other as well the effective translation of research results into actual care. This would be especially aimed at the type A centres (reference centres). **Implementation:** medium-term (2 to 5 years) (once the centre structure has been established) **Responsible bodies:** BMBF, BMG, NAMSE partners, university clinics, non-university research facilities. **Action Field 3: Diagnostics** ***Area:*** ▪ Initial Contact: Primary Care ***Recommendations:*** In order to formulate concrete solutions, NAMSE recommends initiating a survey among primary-care providers to determine the reasons behind the causes of delays in diagnosis at the primary-care level23. NAMSE also recommends that the patients´ path to diagnosis be documented at the centres in order to gain insight into how a diagnosis is reached, the goal being to obtain concrete information on how to expedite diagnostic means. ***Proposed action 17:*** Initiate as part of a pilot project an analysis of what is necessary to ensure cooperation between the centres and primary-care providers (for example, the interface between the centres and primary-care providers). **Implementation:** short-term (1 to 2 years) (once the centre structure has been established) **Responsible bodies:** German Association of General Practitioners, German Society of Paediatrics and Adolescent Medicine (DGKJ). ***Proposed action 18:*** Initiate as part of a pilot project at the centres for rare diseases a questionnaire to document the path to diagnosis from initial contact at the primary-care provider to the respective centre. The goal is to improve the database in order to identify roadblocks in the process and find appropriate solutions. ***Implementation:*** short-term (1 to 2 years) (once the centre structure has been established) **Responsible bodies:** Type A centres (reference centres). ***Area:*** ▪ Diagnostic Software Technologies

	Recommendations: NAMSE assumes that technical aids will serve to facilitate the recognition of patients with rare diseases within primary care as well as to allow the ascertainment of suspected or confirmed diagnoses for a number of rare diseases. For NAMSE this means that, in order to develop such technical aids, it will be necessary to create a complete and uniform coding of rare diseases. It is the hope and expectation of NAMSE that the introduction of the future ICD-11 will proved to be a major step on the road to encoding the majority of these diseases. Until the ICD-11 becomes available, however, NAMSE recommends developing resource-low solutions. A project should investigate the possibility of automatically linking or coupling the alpha-ID of the ICD-10 to the Orpha code number provided by Orphanet. The goal would be to have a clear and uniform codification of the rare diseases available at the Centers for Rare Diseases to be used in research and care activities. In this sense it might also be possible that software algorithms be implemented as part of existing medical practice software in order to point toward rare diseases in the light of certain symptom constellations. NAMSE suggests testing which of the existing software packages would be suitable and how the software manufacturers could integrate rare diseases into their software. NAMSE further recommends the development of research tools for primary-care providers to employ when confronted with certain typical syndromes in order to better classify the disease. In this manner they can point to unusual syndromes early on as being possible rare diseases. ***Proposed action 19:*** A uniform coding scheme for all patients with rare diseases employing the Orpha diagnostic coding system in conjunction with ICD-10 GM and in anticipation of the publication of ICD-11. **Implementation:** short-term (1 to 2 years) **Responsible bodies:** Orphanet Germany, DIMDI, part of the German Federal Ministry of Health. ***Proposed action 20:*** A pilot project to validate software used in primary-care private practices to provide differential diagnostic tools for the diagnosis of rare diseases in addition to more common diseases. Subsequently, existing algorithms need to be (further) developed and implemented into existing software packages. **Implementation:** Pilot project: short-term (1 to 2 years), implementation: medium-term (2 to 5 years) **Responsible bodies:** German Association of General Practitioners, DGKJ. ***Proposed action 21:*** Solicitation of a project for developing a web-based diagnostic tool for primary-care providers. This tool should utilize existing information sources, in particular Orphanet Germany and the foreseen mapping of care facilities for persons with rare diseases (cf. proposed action 38 below). **Implementation:** short-term (1 to 2 years) **Responsible bodies:** Open solicitation. ***Proposed action 22:*** Once the factors leading to delays in the assessment of a diagnosis have been resolved and concrete provisions have been implemented to ensure rapid diagnosis, it should be assessed whether the care given by primary-care and specialist-care providers to persons suspected of having rare diseases but without a confirmed diagnosis is sufficiently reflected in the German Uniform Fee Scale for Medical Procedures (part of the Statutory Health Insurance system). **Implementation:** medium-term (2 to 5 years) **Responsible bodies:** Evaluation Committee on the Uniform Fee Scale for Medical Procedures.

	Area: ▪ Innovative Sequencing Technologies for Molecular Diagnostics ***Recommendation:*** Because of the major importance of genetic diagnostics in the field of rare diseases, patients should have access to the newest methods, inasmuch as these methods can ensure or accelerate the availability of diagnostic means to achieve the patient-oriented optimization of healthcare. NGS technologies should be introduced into the molecular diagnostics of rare diseases once a proper list of indications as well as a specification of services have been prepared and tested to show the conditions and indications under which optimal care can be provided. ***Proposed action 23:*** Take up consultations in the Evaluation Committee on the Uniform Fee Scale for Medical Procedures on the introduction of NGS technologies. **Implementation:** short-term (1 to 2 years) **Responsible bodies:** Health-care providers (preliminary stage), Evaluation Committee on the Uniform Fee Scale for Medical Procedures. ***Area:*** ▪ Guidelines ***Recommendation:*** NAMSE recommends resorting to existing structures and employing these "pragmatically" in order to prepare guidelines for rare diseases. First, a prioritization based on prevalence, medical necessity and feasibility should be established to determine the available expert knowledge of rare diseases. Because the Association of Scientific Medical Societies (AWMF) and the AWMF Institute for Medical Science Management are largely responsible for developing guidelines in Germany, it would seem logical to create any new structures within these institutions to prepare guidelines for rare diseases. NAMSE recommends that the respective professional association be appointed to be responsible for the interdisciplinary preparation of such guidelines. In addition, NAMSE suggests that the absorption of costs involved in preparing such guidelines for rare diseases be examined by the proper entities. NAMSE further suggests that, as a rule, some aspects of the diagnostics or therapy involved in the differential diagnostics of relevant rare diseases be incorporated into existing or new guidelines for widespread diseases. Whenever such guidelines are set to be revised or rewritten, NAMSE recommends that peculiarities or subtypes of existing diseases (or pathophysiologically or symptomatically related rare diseases) be included in the new guidelines. The goal should be that the AWMF, being the leading organization responsible for such guidelines, address this demand as part of all future guidelines. ***Proposed action 24:*** In order to support the development of guidelines for rare diseases, an electronic platform should be established with the expressed intent of setting up such guidelines. These guidelines should be adapted to the needs of the field of rare diseases in consultation with the AWMF. The implementation of an electronic platform serves to save both time and costs, increase the transparency of the procedure and reflect the special needs of patients with rare diseases. **Implementation:** short-term (1 to 2 years) **Responsible bodies:** Technology, Methods, and Infrastructure for Networked Medical Research (TMF, sponsored by the BMBF), AWMF. ***Proposed action 25:*** Carry out a methodological project to develop criteria for the assessment and evaluation of scientific studies with few participants with regard to establishing guidelines. **Implementation:** short-term (1 to 2 years)

	Responsible bodies: AWMF, Institute for Quality and Efficiency in Healthcare. ***Proposed action 26:*** Set up a standard procedure for including rare diseases in the administration of guidelines for widely prevalent diseases. In this case, the professional medical associations that are to list the differential diagnosis methods for rare diseases that are to be taken into consideration **Implementation:** short-term (1 to 2 years) **Responsible bodies:** AWMF. **Cross-sections Action Field:** Registries ***Area:*** ▪ Web-Portal of Registries of Rare Diseases in Germany ***Proposed action 27:*** Set up a web-portal of registries concerning rare diseases in Germany. **Implementation:** short-term (1 to 2 years) **Responsible bodies:** Orphanet Germany and TMF ***Area:*** ▪ Steering Committee of Registry Operators for Exchanging Information on "Registries on Rare Diseases" ***Proposed action 28:*** Establish a steering committee "Registries of Rare Diseases" (for example, operators of registries, experts) in collaboration with the Technology, Methods, and Infrastructure for Networked Medical Research (TMF) and the NAMSE coordinating office. **Implementation:** short-term (1 to 2 years) **Responsible bodies:** BMG, BMBF, NAMSE partners, TMF. ***Area:*** ▪ Development of Software for Establishing a Databank Prototype to Implement and Manage a Disease-Specific Registry for Rare Diseases ***Proposed action 29:*** Develop a prototypical registry for a "Disease-Specific Registries of Rare Diseases" (including a standardized registry for patients without a disease-specific registry, see Proposed Action 32 below) based on the provisions outlined in the draft by the NAMSE working group 'Registries'. This prototype – or individual software modules contained therein – should be adaptable for existing registries. A standardization of all existing registries is desirable. **Implementation:** short-term (1 to 2 years) **Responsible bodies:** BMBF, BMG. ***Area:*** ▪ Registry of "Patients with an Unclear Diagnosis" ***Proposed action 30:*** Organize a workshop to gather and solve open questions concerning a registry for patients with an ***unclear*** diagnosis. **Implementation:** short-term term (1 to 2 years)

	Responsible bodies: Board of spokespersons of the networks for rare diseases sponsored by BMBF, TMF. ***Proposed action 31:*** Depending on the results of such a workshop outlined in proposed action 30 above, implement a project to establish a registry for persons with an unclear diagnosis. **Implementation:** medium-term (2 to 5 years) **Responsible bodies:** NAMSE partners ***Area:*** ▪ Project "Non-Disease-Specific Registry ***Proposed action 32:*** Establish a project "non-disease-specific registry" based on (and thus subsequent to) the development of a prototype registry as suggested in proposed action 29. **Implementation:** long-term (over 5 years) **Responsible bodies:** Steering committee of the previously mentioned registry for rare diseases (proposed action 28). **Action Field 4: Information Management** ***Area:*** ▪ Adequate Patient Information on Rare Diseases ***Recommendation:*** NAMSE recommends preparation of a checklist based on previous criteria in order to examine whether existing information on rare diseases is purposeful, standardized and of high quality. This checklist should serve as the basis for developing patient information for rare diseases. Above all NAMSE recommends revising existing information based on this checklist. ***Proposed action 33:*** Develop a checklist "Criteria for Good Patient Information on Rare Diseases" based on the draft paper prepared by NAMSE. **Implementation:** short-term (1 to 2 years) **Responsible bodies:** ACHSE e.V., Agency for Quality in Medicine (ÄZQ). ***Proposed action 34:*** Prepare a concept for establishing and implementing a checklist "Criteria for Good Patient Information on Rare Diseases" among a broad selection of organizations offering patient information on rare diseases. **Implementation:** short-term (1 to 2 years) **Responsible bodies:** ACHSE e.V., ÄZQ. ***Proposed action 35:*** A joint project by Orphanet Germany and ACHSE e.V. should be conducted to prepare a format for disseminating German-language patient information based on the checklist "Criteria for Good Patient Information on Rare Diseases." **Implementation:** short-term (1 to 2 years) **Responsible bodies:** Orphanet Germany, ACHSE e.V. ***Area:***

	▪ Joint Communications on the Subject of Rare Diseases ***Proposed action 36:*** Develop and implement a concept for joint communications and procedures for public relations in the realm of rare diseases. **Implementation:** short-term (1 to 2 years) **Responsible bodies:** NAMSE coordinating office, ACHSE e.V. ***Area:*** ▪ Central Information Portal ***Recommendations:*** NAMSE recommends setting up a central and integrated information portal on the Internet for rare diseases to disseminate both existing and future information offers on this subject. This portal should meet the following prerequisites: a) Provide existing information on rare diseases, including diagnostic and therapeutic means, patient organizations, treatment and research centres, registries, etc. b) A hotline for persons seeking immediate information could provide a vital service alongside the online opportunities. c) Provide a map of all care offers for persons with rare diseases as part of the information portal. d) Orphanet Germany operates the information platform for rare diseases and delivers information concerning services (expert centres, diagnostic services, patient organizations, clinical studies, patient registries, mutation databases, biobanks, research projects, networks, and so on). In addition, the platform contains articles for both professionals and laypersons with descriptions of rare diseases. Orphanet is an encyclopaedia of relevant disease information. e) Provide all pertinent links to scientific associations, patient organizations, diagnostic or therapeutic facilities (centres). f) The portal (and the hotline) should not provide original materials, but rather refer to the relevant information sources through an appropriate and intuitive user guidance system. ***Proposed action 37:*** Draft a concept including suggestions for funding for the establishment of a central information for rare diseases with the aid of Orphanet resources. **Implementation:** short-term (1 to 2 years) **Responsible bodies:** Orphanet Germany, ACHSE e.V. ***Proposed action 38:*** Orphanet, with the participation of ACHSE e.V. (www.achse.info), should be set up in an information portal to serve as central information platform providing all quality rare diseases. **Implementation:** short-term (1 to 2 years) **Responsible bodies:** Orphanet Germany, ACHSE e.V. ***Proposed action 39:*** Determine the need for a central information hotline as well how which reference system would best meet that need and how much such a system would cost (both with and without the hotline). **Implementation:** short-term (1 to 2 years) **Responsible bodies:** BMG, Orphanet Germany, ACHSE e.V., Independent Patient Counselling Centers of Germany, Federal Association of Self-help Organizations of People with Disabilities and Chronically People and Their Relatives in Germany (BAG SELBSTHILFE e.V.), NAMSE coordinating office.

	Area: ▪ Medical and Dental Training and Continued Education ***Proposed action 40:*** Establish a national, competence-based catalogue of learning objectives such that students of medicine and dentistry become so thoroughly acquainted with the special characteristics of rare diseases with respect to their symptoms, physiology, diagnostics, therapy and care that they acquire the necessary medical competence in all respects (cognitive, applied and emotional/reflective). In addition, students of medicine and dentistry should have all necessary information sources on rare diseases at their disposal. **Implementation:** short-term (1 to 2 years) **Responsible bodies:** German Association of Medical Faculties (MFT) ***Proposed action 41:*** As part of the joint project sponsored by BMBF in the Competence Network for Medicine in Baden-Wuerttemberg, rare diseases with their specific characteristics should be introduced into the curricula of the medical faculties. The results and experiences gathered from this joint project should then be made available to all other federal states so that such actions can then also be implemented by other faculties. **Implementation:** medium-term (2 to 5 years) **Responsible bodies:** Project management of joint project, MFT. ***Proposed action 42:*** Inclusion of questions on rare diseases in the examination questions of the Institute for Medical and Pharmaceutical Examination Questions. **Implementation:** medium-term (2 to 5 years) **Responsible bodies:** BMG, AWMF. ***Proposed action 43:*** The guidelines for continued and advanced training of physicians prepared by the German Medical Association (BÄK) and the German Dental Association (BZÄK) as well as those prepared by the individual state medical associations (LÄK) and the individual state dental associations (LZK) should generally contain information concerning how to address rare diseases. **Implementation:** short- (1 to 2 years) to medium-term (2 to 5 years) **Responsible bodies:** BÄK, BZÄK, LÄK, LZK, professional societies ***Proposed action 44:*** Type A centres (reference centres) and type B centres (centres of expertise) should provide courses in continuing education approved by the state medical associations (LÄK) at regular intervals and in association with the respective patient organizations (inasmuch as present). The goal of these courses is to provide physicians with information on rare diseases and to inform them of existing information sources as well as how to deal with a lack of information. **Implementation:** short-term (1 to 2 years) (once the centre structure has been established) **Responsible bodies:** Type A centres (reference centres) and type B centres (centres of expertise), professional societies. ***Proposed action 45:*** Expand the existing courses in continuing education approved by the respective patient organizations to include other rare diseases. **Implementation:** short-term (1 to 2 years) **Responsible bodies:** ACHSE e.V., patients´ representatives.

	Area: ▪ Public Relations ***Proposed action 46:*** Develop and implement a concept for public relations activities with respect to NAMSE and to the realization of a Nation Action Plan. **Implementation:** short-term (1 to 2 years) **Responsible bodies:** NAMSE coordinating office. ***Area:*** ▪ Telemedicine ***Proposed action 47:*** Identify and evaluate tele medical offerings for rare diseases. **Implementation:** short-term (1 to 2 years) **Responsible bodies:** Joint representatives from the various centres, TMF, Association of Insurance Science and Practice e.V.: Committee on Telemedicine. **Cross-sectional Action Field: Patient Orientation** ***Areas:*** ▪ Research ***Proposed action 48:*** Include as appropriate the experiences gathered by patient organizations in the development and implementation of patient-oriented research and healthcare projects on rare diseases. **Implementation:** short-term (1 to 2 years) **Responsible bodies:** BMBF, DFG, BMG ***Area:*** ▪ Expert Opinions by the Medical Advisory Service of the German Statutory Health Insurance **Proposed action 49:** Improve the transparency surrounding the role and advisory capacity of the Medical Advisory Service of the German Statutory Health Insurance (MDK). To this end, the Medical Advisory Service of the Federal Association of Health Insurance Funds (MDS) can serve as contact point for patient organizations at the national level and can assume any necessary coordinating functions in the MDK community. **Implementation:** short-term (1 to 2 years) **Responsible bodies:** Central Association of Statutory Health Insurance Funds, MDS. ***Area:*** ▪ Support and Qualification of Patient Organizations

	Proposed action 50: Within the limits of existing legal regulations, the NAMSE partners shall work to ensure the appropriate support for the activities of the patient organizations and their qualification. Implementation: short-term (1 to 2 years) **Responsible bodies:** BMG, ACHSE e.V., BAG SELBSTHILFE e.V. ***Area:*** ▪ European Networks ***Proposed action 51:*** Provide support for integrating national patient organizations into Europe-wide cooperation's concerning rare diseases. **Implementation:** short-term (1 to 2 years) **Responsible bodies:** BMG, the Patient organizations. **Action Field 5: Implementation and Future Development** ***Proposed action 52:*** Even after passage of the National Action Plan NAMSE should continue its efforts with the collaboration of all previous partners, the goal being to evaluate and follow-up in due time the implementation of the Action Plan. To this end, the necessary structures and processes (for example, Steering Committee, coordinating office, and means of communication) should be addressed in a separate organizational concept. **Implementation:** after passage of the National Action Plan **Responsible bodies:** BMG, BMBF, ACHSE e.V.
Governance and organisational structures	People with Rare Diseases was founded at the behest of the German Federal Ministry of Health. Together with the BMBF and the Alliance of Chronic Rare Diseases, NAMSE became a national council responsible for coordinating and publishing the common efforts. The primary goal of NAMSE is to prepare suggestions for establishing a National Action Plan for People with Rare Diseases by 2013 as well as supporting the establishment of national centres of expertise. The Action League shall contribute to implementing the Recommendation of the Council of the European Union. This includes: ▪ drafting a National Action Plan for Rare Diseases ▪ implementing and monitoring this Plan ▪ supporting the establishment of centres of excellence. The Action League is intended to coordinate measures for improving the health situation of persons with rare diseases and initiate pilot projects and further action in the field of rare diseases (for partners of the Action League see additional information). Additionally responsible bodies are outlined for each action (see implementation actions).

Funding model	Type A, Type B and Type C centres are to be funded by the existing legal framework. The following were discussed in detail with respect to their suitability for funding the three types of centres of expertise: (1) Highly specialized outpatient care (§116b Social Code Book V) (2) care by panel doctors and dentists (§§95ff Social Code Book V) including care provided by hospital physicians or clinics authorized to provide outpatient care (§§116, 116a Social Code Book V) (3) enabling provisions for university outpatient clinics (§117 and 120 Social Code Book V) as well as social-paediatric centres (§119 Social Code Book V). In addition, besides the collective agreements, there are the selectively contracted conditions for remunerating special services within the framework of integrated care (§§140a ff Social Code Book V) or specialized medical care (§73c). However, selectively contracted solutions have proven to be unsuitable for ensuring universal access to care for the small numbers of persons affected because of the specific challenges faced in the area of rare diseases. Instead, the existing funding possibilities offered by collective contracts are to be used to finance the systematic implementation of the three-tiered structure of centres for rare diseases. The NAMSE partners will urge that the necessary funds that are not already included in the existing standard remunerations be made available by the payers. This funding will be assessed in proposed action 1 whereby representatives of patient interests will work together with representatives of both healthcare providers and the third party payers to clarify the common criteria and requirements for funding centres. Funding will be reviewed (2 years after implementation) to determine whether the funding elements contained in the existing standard remunerations are sufficient to fund the centres of expertise (2 years after implementation) in proposed action 3. Other specific mentions related to funding are: ▪ diagnostic test systems are developed and employed at the research level will have to be funded through public subsidies ▪ investigator-initiated trials (IIT) are presently being funded by the BMBF and the DFG ▪ the BMBF has funded ELSA research since 1997 and proposed action 13 is to continuing this funding ▪ the ERA-Net Initiative "E-Rare" collects information about research going on into rare diseases in countries, to strategically coordinate activities and to fund transnational research projects. Germany is a partner and proposed action 15 aims to continue this research funding ▪ funding and support for research is also identified as proposed action 16.
References and or links to other initiatives	(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)
Screening programmes (including newborn screening)	*Screening is not specifically mentioned.*
Personalised medicine, genomics, genetic counselling	Yes, within the Action Field Research, the Area Aetiology and Genome Analysis is outlined with associated recommendations and actions. Additionally, within the Action Field Diagnostics the Area Innovative Sequencing Technologies for Molecular Diagnostics it outlined with associated recommendations and actions.
Models of care/care pathways	NAMSE recommends the establishment of centres for rare diseases at three different, cross-linked levels of specialization. These levels are not to differ in the quality of the care they provide, but only in the spectrum of services they offer. They are to be embedded in the local healthcare structures in both primary and specialist care. The three levels of specialization in the model of cross-linked centres for rare

	diseases are to be differentiated according to whether the treatment they offer is outpatient/inpatient or disease (group) specific/non-disease specific. The type C centres (cooperating centres for a specific rare disease/disease group x) are to be responsible for disease-specific or disease-group specific, interdisciplinary and multi professional outpatient care. A type C centre (cooperating centre) is to be primarily concerned with delivering concrete care for patients with a confirmed diagnosis or a clear suspected diagnosis. Type C centres may include non-hospital subspecialized practices, group practices, medical care centres or hospitals. Type B centres (centres of expertise for a specific rare disease or disease group x) are also to be organized around certain specific rare diseases or rare disease groups for patients with a confirmed diagnosis or a clear suspected diagnosis. However, they are to offer not only outpatient but also inpatient, interdisciplinary and multiprofessional care. Thus, the type B centre (centre of expertise) is to be an established hospital that is equipped to deal with a specific rare disease or rare disease group both on an inpatient and an outpatient basis. Type A centres (reference centres for rare diseases, with centres of expertise for xyz)10 are to consist of more than two type B centres (centres of expertise) and offer, in addition, special non-disease specific structures (for example, for the treatment of patients with unclear diagnoses, patient guides, interdisciplinary case conferences, innovative special diagnostics). Type A centres (reference centres) are to be the referral centre for patients with an unclear diagnosis; they are also to do basic and clinical research and they are entitled to provide training tools and training sessions covering the medical dimension of care for undergraduate medical students at medical school. Within the Action Field the Area Center Model for Rare Diseases outlines how type A centres should: ▪ guide patients with specific diagnostic or therapeutic needs to their proper place within the system (seamless patient pathway and, if necessary, national and Europe-wide routing). This is also outlined as part of the criteria for Type A, Type B and Type C centres. Within the Action field of Diagnostics information is provided on plans to improve the treatment pathway for people diagnosed with a rare disease (See above Proposed Action 17 and 18).
Workforce	Yes, within the Action Field Information Management, Area Medical and Dental Training and Continued Education is outlined along with associated recommendations and actions (see Implementation actions). Training for patient organisations is also outlined as an Area (Support and Qualification of Patient Organizations) within Action Field Patient Orientation (see implementation action). Training and teaching are also outlined within the criteria for Type A, Type B and Type C centres.
European Reference Network	*Yes. Listed as an individual non-disease specific interdisciplinary tasks of the type A centre (reference centre):* ▪ To participate in the European reference networks for rare diseases in accordance with the provisions of Directive 2011/24/EU of the European Parliament and the European Council ▪ To provide standardized methods of diagnosis for patients with an unclear diagnosis who demonstrate a high probability of having a rare disease. Type a centres also participate in remote diagnostic procedures (for example, telemedicine, teleconsultation, symposia to review unclear diagnoses and standard operating procedures between the centres; the latter are especially important with respect to the role of the European reference networks).

Health information (including rare disease registries)	*Yes. Registries is identified as an Action Field (see themes or priorities) and therefore has a number of associated recommendations and actions within different areas.* *Yes. Information Management is identified as an Action Field (see themes or priorities) and therefore has a number of associated recommendations and actions within different areas.* *Additionally, within Action Field: Diagnostics, Area Diagnostic Software Technologies a uniform coding scheme is outlined as a Proposed action 19.*
Orphan medicines	*Yes. Orphan drugs, off-label use and evidence generation is outlined as an Area within the Action Field: Care, Centres and Networks (see implementation actions).*
Rare disease research	Mentioned heavily throughout. Also Research is identified as an Action Field (see themes or priorities) and therefore has a number of associated recommendations and actions within different areas. The research landscape in Germany with respect to rare diseases has many facets but lacks a consistent structure. Research is presently done where local interests call for it and is directed mainly toward individuals and not toward structural units. There are indeed a number of good and very good initiatives, harbouring local expertise and activities; yet there is little overarching coordination of these activities. A further important phenomenon is that only a marginal part of the estimated 7,000 to 8,000 known rare diseases have been researched to any depth. The following actions serve to intensify general research into rare diseases in the areas of fundamental research, clinical research and health services research as well as to improve the overall structural conditions of research into rare diseases. Also identified as an Area within Action Field Patient Orientation (see implementation actions). Type A centres are also outlined to do basic and clinical research and are entitled to provide training tools and training sessions covering the medical dimension of care for undergraduate medical students at medical school.
Alignment beyond the healthcare sector	Appears to be focused around health mainly. However, does refer to Ethical, Legal and Social Aspects as an Area within the Action Field Research. Also does acknowledge that rare disease diagnosis affects many social aspects of a patient´s life such as schooling, career choice, partner choice, family planning and legal manifestations. Also within the action field Information Management a plan to implement public relations a with respect to NAMSE and the Nation Action Plan is mentioned. (See above proposed action 46).
Any additional information (for example, background to the strategy or strategy development)	In 2010, the BMG, together with the BMBF and ACHSE e.V., founded the NAMSE. NAMSE's goal is to improve the life situation of each and every individual with a rare disease through a concerted effort. At the end of a three-year co-ordination process, which required the commitment of all of those involved in the healthcare sector, a total of 52 proposals for action were compiled and included in a National Plan of Action for People with Rare Diseases. Partners of NAMSE (in German): ▪ Allianz Chronischer Seltener Erkrankungen e.V. (ACHSE e.V.) ▪ Arbeitsgemeinschaft der Obersten Landesgesundheitsbehörden (AOLG), represented by the respective federal state holding the chair ▪ Arbeitsgemeinschaft der wissenschaftlichen medizinischen Fachgesellschaften e.V. (AWMF) ▪ Beauftragter der Bundesregierung für die Belange der Patientinnen und Patienten

	▪ Bundesarbeitsgemeinschaft Selbsthilfe von Menschen mit Behinderung und chronischer ▪ Erkrankung und ihren Angehörigen e.V. (BAG SELBSTHILFE e. V.) ▪ Bundesärztekammer (BÄK) ▪ Bundesministerium für Arbeit und Soziales (BMAS) ▪ Bundesministerium für Bildung und Forschung (BMBF) ▪ Bundesministerium für Familie, Senioren, Frauen und Jugend (BMFSFJ) ▪ Bundesministerium für Gesundheit (BMG) ▪ Bundespsychotherapeutenkammer (BPtK) ▪ Bundesverband der Pharmazeutischen Industrie e.V. (BPI) ▪ Bundesverband Medizintechnologie e.V. (BVMed) ▪ Bundeszahnärztekammer (BZÄK) ▪ Deutsche Forschungsgemeinschaft (DFG) ▪ Deutsche Krankenhausgesellschaft e.V. (DKG) ▪ Deutscher Hausärzteverband e.V. ▪ Deutscher Pflegerat e.V. (DPR) ▪ Gemeinsamer Bundesausschuss (G-BA) ▪ GKV-Spitzenverband ▪ Kassenärztliche Bundesvereinigung (KBV) ▪ Kassenzahnärztliche Bundesvereinigung (KZBV) ▪ Medizinischer Fakultätentag der Bundesrepublik Deutschland (MFT) ▪ Orphanet-Deutschland ▪ Verband der privaten Krankenversicherung e.V. (PKV) ▪ Biotechnologie im Verband der forschenden Pharma-Unternehmen (vfa bio) ▪ Verband der Universitätsklinika Deutschlands e.V. (VUD) ▪ Verband der Diagnostica-Industrie e.V. (VDGH). A specific list of criteria to be met in the three tiered centre model is provided in the document, however was not extracted as not deemed relevant.

Key: ACHSE e.V.: Alliance for Chronic Rare Diseases; AWMF: Association of Scientific Medical Societies; ÄZQ: Agency for Quality in Medicine; BAG SELBSTHILFE e.V.: Federal Association of Self-help Organizations of People with Disabilities and Chronically People and Their Relatives in Germany; BÄK: German Medical Association; BMBF: the German Federal Ministry for Education and Research, BMG: the German Federal Ministry of Health; BZÄK: German Dental Association; DFG: German Research Foundation; DGKJ: General Practitioners, German Society of Paediatrics and Adolescent Medicine; DKG: German Hospital Federation; DIMDI: German Institute for Medical Documentation and Information; ELSA: ethical, legal and social aspects; EU: European Union; G-BA: the Federal Joint Committee of Physicians and Health Insurance Funds; GKV-Spitzenverband: Federal Association of Statutory Health Insurance Funds; LÄK: individual state medical associations; LZK: individual state dental associations; MDK: Medical Advisory Service of the German Statutory Health Insurance; MDS: Federal Association of Health Insurance Funds; MFT: German Association of Medical Faculties; NAMSE: National Action League for People with Rare Diseases; NGS: next generation sequencing; TMF: Technology, Methods, and Infrastructure for Networked Medical Research; VUD: Association of University Clinics in Germany.

Table B14. Data extracted for Germany (NAMSE interim review)

Germany	Strategy information
Author(s) **Title**	National Action League for People with Rare Diseases (NAMSE) Interim report on the implementation of the National Action Plan for People with Rare Diseases[31]
Timeline	Published March 2017.
Overall aim(s)	This document is intended to provide an overview of the current implementation status and the achievement of the objectives of the measures and projects formulated in the national action plan.
Themes and or priorities	As this is a progress review the themes and or priorities or action fields are the same as the original plan.
Targets (if specified) and measurement method(s) (where available)	*None mentioned.*
Implementation action(s), lead(s) and key performance indicator(s)	The implementation status of the proposed actions are outlined below: **Action Field 1: Care, centres, and networks** ***Area:*** ▪ The Center Model for Rare Diseases **Proposed Actions 1, 2 and 3:** The criteria for Type A and Type B centres were specified by the Recognition Process Working Group and agreed upon by the alliance partners at the steering group meeting on June 4, 2014. The development of a catalog of requirements for Type C centres (collaboration centres) will be postponed for the time being. A NAMSE core group was then set up with the aim of developing a proposal for future institutional governance and, with external expertise, a certification process for RDS centres based on the centre model of the National Action Plan. This described the tasks and requirements for the committees (executive (compliance monitor), legislative (standard setter) and judiciary (norm decision-maker)) of a future procedure. At the same time, the requirements catalogs developed and agreed upon by NAMSE for Type A centres and Type B centres were tested in a pilot phase. For this purpose, the AG Centers for Rare Diseases, founded in September 2014, was involved. This is made up of representatives from existing centres for rare diseases. The heads of the centres have filled out the requirements catalogs with information about your facility and evaluated them for practicality, plausibility and completeness. Based on the feedback from the centres, the core group revised the requirements catalogs again. In this step, the requirements were also divided into quality objectives and core criteria. At the end of 2015, the requirements catalogs for Type A and Type B centres were approved by the members of the steering group agreed upon and published on the NAMSE website. Discussions have taken place with certification bodies regarding the implementation of a corresponding procedure based on the requirements catalogs agreed upon in NAMSE. Currently a NAMSE working group is examining how the recognition process could be

	integrated into a sustainable NAMSE structure. The formation of centres and formation of European reference networks (ERN) in the field of rare materials diseases is also a central requirement of the European Council recommendation for measures in the field of rare diseases from 2009, confirmed by the EU directive 2011/24/EU on the exercise of patients' rights in cross-border patient care. The call for proposals for the European reference networks was published in March 2016. The ERNs are expected to start working by March 2017. In addition to the implementation of the centre model, Proposed Action 1 also includes the analysis of possible financing channels. For this purpose, the Federal Association of Statutory Health Insurance Funds (GKV-SV) carried out an analysis of the financing of the centres in the status quo, including within the framework of the university outpatient clinics and socio-paediatric centres, which are already a contact point for people with rare diseases. For this purpose, the GKV-SV coordinated and implemented extensive collaborations on data consolidation and analysis with the health insurance companies and the associations of the types of insurance companies. However, generating the data has turned out to be more complicated than initially assumed, so no results are available yet. At the same time, Association of University Clinics in Germany (VUD) and German Hospital Federation (DKG) wanted to use questionnaires at selected university hospitals to collect routine data about which service areas are currently not adequately funded. Here too, the response from the centres surveyed was not satisfactory due to the organizational complexity of the facilities. At the same time, the Hospital Structure Act was passed, which specifies the existing regulations on centre surcharges. It is planned that the specific tasks that can be financed with centre surcharges will be carried out by the National Association of Health Insurance Funds and the Association of Private Health Insurance together with the German Hospital Association (contracting parties at the federal level). The special tasks can arise in particular from: a) a supra-regional and cross-hospital performance of tasks, b) the need for special provisions of a hospital, especially in centres for rare diseases, or c) the need to concentrate care at individual locations due to exceptional circumstances -usual technical and personnel requirements. The special tasks must be identified in the hospital plan of the respective country or based on a similar definition. The legal deadline for specifying the special tasks of centres expired on March 31, 2016. The contracting parties at the federal level were unable to conclude an agreement in accordance with Section 9 Paragraph 1a No. 2 KHEntgG in several rounds of negotiations from January to July 2016. The National Association of Health Insurance Funds has therefore declared the failure of the negotiations and appealed to the Federal Arbitration Board in accordance with Section 18a Paragraph 6 KHG. On December 8, 2016, the arbitration board was appointed to the agreements on the special tasks of centres. Centers for rare diseases must comply with the requirements of the NAMSE. The requirements catalogs with core criteria and quality objectives for type A and type B centres must be taken into account. In order to examine the processes and developments of individual proposed measures in the National Action Plan, the Federal Ministry of Health has been funding the project "Scientific Support of the National Action Plan for People with Rare Diseases (WB_NAPSE)" (measure proposal 3) from the beginning of 2015 until the end of March 2017. ***Area:*** ▪ Orphan Drugs, Off-Label Use and Evidence Generation **Proposed Actions 4, 5, 6 and 7:** Measure proposal 4 is intended to demonstrate the need for measures to optimize the supply of medication to people with RD after the centre model has been established. Measure proposal 5 provides for a healthcare research study on the care of patients with RD with orphan drugs during inpatient hospital treatment and an inpatient rehabilitation stay, regardless of

	whether they were caused by RD or not. The aim is to disclose possible problems in the financing of orphan drugs and, if necessary, to derive additional measures from them. The prerequisite for the implementation of both proposed measures is the formulation of scientific questions. A technical discussion on healthcare science could be considered for this purpose. There were already initial preliminary considerations for the conceptual planning of the technical discussion. In order to improve the supply of medicines for RD, the NAMSE recommends in the National Action Plan to investigate the extent of off-label use in RD using data from the routine care of patients with approved medicines. In order to generate the best possible evidence on this question, a project financed by the German Federal Ministry of Health (BMG) until March 31, 2017 to record the extent of off-label use in RD is being carried out by the BfArM in collaboration with the German Institute for Medical Documentation and Information (DIMDI) (measure suggestions 7ab). The analysis procedures for off-label applications of drugs in RD and non-RD are now established as regular procedures. In the first half of 2016, 26 active ingredients from 5 active ingredient groups (antithrombotic, immunosuppressant's, antiepileptics, antidepressants, antineoplastic) were examined. A total of around 180 active ingredients will be analysed. The data obtained can be used to carry out the follow-up activities 7c (G-BA consultation and commissioning of the off-label expert groups in accordance with Section 35c Para. 1 SGB V) and 7d contained in the proposed measure 7 (Establishment of the infrastructure for clinical trials for approved drugs for use in RD). The project based on the proposed measures 7ab is one of the first and by far the most extensive of its kind to examine the database created at DIMDI as a result of the Data Transparency Ordinance. The first investigations of the proposed measures 7ab have answered the question of proposed measures 6: In principle, it is possible to obtain objective findings on off-label use for RD and non-RD from data from the routine care of patients with approved drugs and drugs according to the DaTraV to win. **Action Field 2: Research** ***Area:*** ▪ Etiology and Genome Analysis **Proposed Action 8:** For the efficient use of high-throughput procedures and genome analyses, NAMSE recommends the establishment and expansion of selected sequencing centres for RD, primarily at type A centres (reference centres) (measure proposal 8). The measure is linked to the establishment of the NAMSE centre structure. ***Area:*** ▪ Pathophysiology and Disease Mechanisms **Proposed Action 9:** the funding of research projects that also include the establishment of animal and cell models to elucidate the pathophysiology of RD, will be implemented as part of ongoing funding procedures by the German Federal Ministry for Education and Research (BMBF) and the German Research Foundation (DFG). The following initiatives should be highlighted: - The funding of 10 translation-oriented national research associations 2015/2016 with approx. 20 million euros for 3 years.

	- Funding as part of the ERA-Net E-Rare: from the 2014 announcement on innovative therapeutic procedures in animal and cell models, 14 transnational projects, 9 of which have German participation, are being funded by the BMBF with €2.7 million. From the announcement in 2015, 19 transnational projects, 17 of which with German participation, will be funded by the BMBF and DFG with €5.4 million from 2016. A new announcement on "Funding clinical research for the new use of already known drugs (repositioning) in rare diseases" was published at the beginning of 2016 with the participation of the BMBF and DFG. As part of this call for proposals, which the DFG took part in on with the BMBF contributing €3.0 million, will support, among other things, preclinical studies on animal models. ***Area:*** ▪ Development of Diagnostic Test Systems **Proposed Action 10:** Measure proposal 10, intensifying research into diagnostics development in RD, is also being implemented by the BMBF as part of the funding of associations for RD and E-Rare projects. In addition, in all DFG funding procedures it is still possible to apply for funding applications for new diagnostic procedures from SE. In addition, in 2013, the DFG set up a permanent funding offer for confirmatory clinical studies ("Clinical Studies" funding program), which explicitly also includes diagnostic studies. The program is not disease-specific and is therefore open to all rare diseases. One focus of the funding is on novel therapeutic and diagnostic procedures. ***Area:*** ▪ Investigator-Initiated Trials: Prospective, Controlled Clinical Studies **Proposed Action 11:** The specialization of clinical study units on the special requirements of studies on RD depends on the establishment of the centre structure. The measure is not yet being implemented. ***Area:*** ▪ Health Services Research **Proposed action 12a and 12b:** On January 7, 2015, a multidisciplinary healthcare science discussion took place in Berlin (measure proposal 12a). In order to enable a differentiated, professional exchange, representatives of various players in the healthcare system - sponsors, science, service providers, payers, industry, political decision-makers - formed the group of participants. The further procedure for promoting concepts for linking care and research at individual locations, close cooperation between basic research and clinical research as well as accelerating the transfer of new findings into care practice (measure proposal 16) depends on the Establishment of the three-tier NAMSE centre model. As part of the planned recognition process for centres for RD, corresponding research tasks were taken into account in the core criteria for recognition as a centre, which were funded by the relevant research funding organizations in 2013. In total there are over 1,000 projects that deal with the causes, diagnoses and therapies of rare diseases. An analysis of these projects has been published. The aim of the expert discussion was to identify urgent topic areas and research questions in the care of people with rare diseases in Germany. The first topic areas were identified in the technical discussion. Looking back, however, it became clear from the results that the topic areas formulated were mostly general questions about the care situation and structure, which are also relevant for common illnesses, but do not have any RD specificity. In a next step, the participants were asked to supplement the formulated topic areas with concrete examples and questions relating to rare diseases. This specification (on RD specificity) is an important step towards the further development of health services research in rare diseases. The responses were brought together by the NAMSE office. The fact that there

	are already a number of opportunities for health services research on rare diseases was demonstrated in the expert discussion by presenting various existing or planned funding offers in the area of health services research. These include both RD-specific measures such as model projects as well as general measures such as individual projects, junior academies, cooperation networks, and the establishment of research-related registers or the innovation fund as part of the Supply Strengthening Act. In addition, the Kindness for Kids Foundation established an endowed professorship for health services research for rare diseases in children in 2014. A central result that was unanimously highlighted in the expert discussion was that the structural connection of health services research to centres for rare diseases and other organizations that have collaborative relationships with centres for RD must be promoted. The integration of health services research at centres for RD should be established within the framework of the NAMSE centre model (measure proposal 12b). ***Area:*** ▪ Ethical, Legal and Social Aspects (ELSA) **Proposed Action 13:** The ELSA funding programs, which deal with the ethical, legal and social aspects of modern life sciences, are being continued on an ongoing basis by the BMBF. ***Area:*** ▪ Cooperation Between Academia and Industry **Proposed Action 14:** To set up a cooperation platform between academia and an exchange took place between the NAMSE office, the BMBF and industry. In this conversation, existing initiatives were presented and discussed. The plan is to discuss any outstanding questions and how to proceed in a technical discussion. A small group of experts is planned who can contribute experience from existing initiatives. The Alliance for Chronic Rare Diseases (ACHSE) is involved as a representative of patient self-help. The aim of the discussion is to find out how existing platforms can be used sensibly for drug development for rare diseases and which factors are currently leading to initiatives not being used. ***Area:*** ▪ Cooperation with International Partners **Proposed Action 15:** In order to expand international cooperation for successful research on RD, applications can be submitted to the DFG on an ongoing basis within the framework of existing bilateral agreements (for example, DFG-ANR, DACH agreement). In addition, the DFG continues to be involved in the ERANet E-Rare-3 (two more calls are pending). E-Rare-3 is also a member of International Rare Diseases Research Consortium (IRDIRC). In addition, German parts of an international study can also be funded as part of the DFG "Clinical Studies" funding program. The BMBF also supports research funding for international cooperation in RD through participation in the ERA-Net E-Rare and through participation in the IRDiRC). The National Action Plan stated that research on RD in Germany is not sufficiently structured and there is a lack of comprehensive coordination. Research is often not based on need, but rather on local expertise. Better structuring should be achieved by setting up centres for RD. As a basis for further strategic planning, an inventory of the research situation at RD was recommended. The IGES Institute has listed all projects on behalf of the BMBF which were funded by the relevant research funding organizations in 2013. In total there are over 1,000 projects that deal with the causes, diagnoses and therapies of rare diseases. An analysis of these projects has been published.

	Area: ▪ Establishing Centers for Rare Diseases **Proposed Action 16:** The further procedure for promoting concepts for linking care and research at individual locations, close cooperation between basic research and clinical research as well as accelerating the transfer of new findings into care practice (measure proposal 16) depends on the Establishment of the three-tier NAMSE centre model. As part of the planned recognition process for centres for RD, corresponding research tasks were taken into account in the core criteria for recognition as a centre. **Action Field 3: Diagnostics** ***Area:*** ▪ Initial Contact: Primary Care **Proposed Action 17 and 18:** There are currently no results available for measure proposal 17, the analysis of requirements for collaboration between centres and primary care providers. The first starting points can be gained through the BMG-funded project "DENIES Diagnosis Pathways for Rare Diseases in Primary Care". The main objective of the project is to provide and convey in-depth knowledge about the patient's diagnostic journey from the initial contact with the primary care provider to a specialist centre and back to the primary care provider. The focus of the investigation is on the question of how the diagnostic path from the family doctor to the specialist centre and back again is influenced if a patient is suspected of having a rare disease. In this context, influencing factors should be identified that have a positive or negative influence on the diagnostic process. The project ended in November 2015. The final report is currently being prepared. In addition to proposed measure 17, the analysis of requirements for cooperation between centres and primary care providers, a questionnaire should be implemented at RD centres to document the diagnostic path from the initial contact with the primary care provider to the centre. For this you will find a questionnaire on the medical history for CSE patients at the Hannover Medical School application (measure proposal 18). ***Area:*** ▪ Diagnostic Software Technologies **Proposed Action 19:** With the DIMDI project "Coding of Rare Diseases" measure proposal 19 of the action plan implemented. It is financed by the Federal Ministry of Health. The project aims to enable uniform, standardized and simplified coding of rare diseases in Germany using the ICD-10-GM, the alpha-ID and the Orpha identification number. The coding people should not have to operate two classification systems separately. Double coding offers the opportunity to improve the documentation of rare diseases and thereby achieve appropriate recognition of SE in the healthcare system. In addition, the Orpha identification numbers enable a European comparison of the reference networks to be established. On October 11, 2016, DIMDI published the Alpha-ID version 2017 and the Alpha-ID-SE version 2017 as a test file. The sample data set is a free excerpt from this Alpha-ID-SE. Since its last publication in the third quarter of 2016, it has contained around 3,600 entries on rare diseases.

	The file should also be used for other NAMSE measures and projects, for example in the open source register system for RD (OSSE) and the se-atlas. As part of the recognition process for RD centres, it is also suggested that the ICD-10GM Alpha-ID/Orphacode file should be used routinely in order to enable clear, general identification of rare diseases. An evaluation of the project was carried out. This showed that users of the file produced are satisfied with the project's approach and support it. The DIMDI is also involved in an EU project. Partial results have already been published on the project website (www.rd-action.eu). A follow-up project, "Coding of Rare Diseases 2" started in July 2016 and follows this. The aim is a long-term, joint application of ICD-10-GM and the Orpha identification number a standardized file. **Proposed Action 20:** envisages a pilot project to validate practice software that offers differential diagnostic tools, with the question of the extent to which RD is also reflected in addition to common diseases. The general practitioner association has held discussions with a number of companies that want to develop corresponding software or have developed initial approaches. No further results are available at this time. **Proposed Action 21:** development of a diagnostic tool for primary care providers, is covered by the "Computer-aided Diagnostics" project of the Medical School together with Improved Medical Diagnostics IMD GmbH, funded by the Robert Bosch Foundation. In the "Computeraided Diagnostics" project, a questionnaire-based concept is being developed using technologies from the field of data mining in order to shorten the diagnosis of rare diseases. In interviews, people with rare diseases have the opportunity to report on their experiences before their diagnosis. The insights gained through the systematic qualitative evaluation of the reports are incorporated directly into the future questionnaire via a self-learning data mining system. Based on the answers from people with known rare diseases who answer the questionnaire, a new type of data mining system can be trained and then, in the next step, assign questionnaires from people without a diagnosis. The questionnaire has been completed, the results are currently being analysed and then prepared for publication. In the future, this will help guides at centres for rare diseases or doctors in private practice, for example, with the challenge of clarifying the suspicion of a rare disease in people and thus shortening the path to diagnosis. **Proposed Action 22:** The results of the outlined projects DENIES and "Computer-aided Diagnostics" can contribute to the implementation of the first part of proposed measure 22. This stipulates that at the primary care level, factors that lead to a delay in diagnosis have been excluded and measures to accelerate diagnosis have been implemented. Depending on this, the second part of proposed measure 22 is the examination of whether the uniform assessment standard adequately reflects the primary care and specialist care of patients with suspected RD and at the same time an unconfirmed diagnosis. As part of the ongoing German Uniform Evaluation Standard (EBM) reform, the National Association of Statutory Health Insurance Funds is examining the extent to which there is a need for adjustments in the general medical and specialist care of patients with suspected RD and, if there is a possible need for action, suggestions for adapting the EBM are being submitted to the evaluation committee. The decision on the EBM reform is currently scheduled for 2017. ***Area:*** ▪ Innovative Sequencing Technologies for Molecular Diagnostics.

	Proposed Action 23: stipulates that discussions on next generation sequencing (NGS) technology be taken up in the evaluation committee. At its 372nd meeting on March 11, 2016, the evaluation committee decided on the fundamental revision and reassessment of genetic performance in the EBM, which came into force on July 1, 2016. The central aspects of the further development were the adaptation of these services to the state of science and technology as well as the consideration of the special requirements for the genetic diagnosis of rare diseases. With this decision, "high-throughput sequencing" for the diagnosis of RD was included in the EBM. ***Area:*** ▪ Guidelines **Proposed Action 24:** **Proposed Action 25:** In order to adapt an electronic platform for creating guidelines to the requirements of RD, a test run was carried out with a guideline on Pompe disease. The results are not yet available. Under the title "Assessment and evaluation of studies in rare diseases", the Institute for Quality and Efficiency in Health Care has published a report ("Rapid Report") commissioned by the BMG4 (measure proposal 25). The results include that for clinical, patient-oriented research into rare diseases it is particularly important to work in networked supra-regional or international structures. Disease registers play a central role here. In order to serve as a basis for high-quality, clinical, especially non-randomized studies, such disease registries must meet clear quality criteria regarding completeness and completeness. **Proposed Action 26:** The introduction of a regular RD checkpoint in the development of guidelines for highly prevalent diseases was initiated at the Association of Scientific Medical Societies. **Cross-sectional Action Field:** Registries ***Area:*** ▪ Web-Portal of Registries of Rare Diseases in Germany **Proposed Action 27:** provides for the creation of a central, national directory of existing registers. The development of such a web portal, a kind of "telephone book for registers", should be discussed in the Register strategy group (see MV 28). ***Area:*** ▪ Steering Committee of Registry Operators for Exchanging Information on "Registries on Rare Diseases" **Proposed Action 28:** With the aim of increasing the quality and interoperability of national registries in the long term, the "Register for Rare Diseases" strategy group was established (measure proposal 28). The Strategy group serves as an expert panel and communication platform for existing and new users and as a national contact for inquiries from other countries (for example, EU-COM / ISPRA). It is intended to take into account developments at national and international levels in order to develop recommendations for national initiatives. Another work assignment is to develop recommendations for a minimum set/metadata repository of data elements. This directory should contain elements that can be queried in different registers and thus serve interoperability. It is planned to prepare a publicly accessible position paper in which already existing standards are analysed and a statement is made on further topics (for example, proposed measures 30 to 32).

	Area: ▪ Development of Software for Establishing a Databank Prototype to Implement and Manage a Disease-Specific Registry for Rare Diseases **Proposed Action 29:** The project "OSSE - Open Source Registry System for Rare Diseases" is an essential part of the implementation of the measures from the Register field of action, in particular Measure Proposal 29, the development of a model register for disease-specific registers for RD. OSSE provides patient organizations, doctors, scientists and other users with open source software to develop their own patient register or to connect existing registers to the national register interface using a "bridgehead". This will improve the German registry landscape and then also comply with the European guidelines regarding minimum data sets, data quality, and so on (see EUCERD Recommendation on RD Registries). At the same time, the necessary interoperability is achieved, which requires the federation of such registers allowed at national and international levels (for example, decentralized searches that comply with data protection). Since the beginning of 2015, the first available version of the OSSE register software has been available to download free of charge from the website. ***Area:*** ▪ Registry of "Patients with an Unclear Diagnosis" **Proposed Action 30 and 31:** A workshop to collect and clarify open questions regarding a register for unclear diagnoses (measure proposal 30) took place in November 2013. The results of the workshop will be evaluated by the Register strategy group. At the same time, the "VarWatch" project, funded by the BMBF, was launched in the summer of 2015 under the leadership of the Christian Albrechts University in Kiel and with the support of the Technology, Methods, and Infrastructure for Networked Medical Research "Molecular Medicine" working group. The plan is to use VarWatch to build a database of genetic variants found in patients with syndromic disorders of unclear etiology. Over the next two years, work will be done to establish VarWatch technically, to make it known to potential users and to develop a concept for long-term operation (measure proposal 31). ***Area:*** ▪ Project "Non-Disease-Specific Registry" **Proposed Action 32:** A non-disease-specific registry should be developed for SEs that are so rare that a separate registry does not seem useful. It is planned that this register will be based on the technology of the OSSE model register. The aforementioned Register strategy group is responsible for implementation (measure proposal 32). **Action Field 4: Information Management** ***Area:*** ▪ Adequate Patient Information on Rare Diseases **Proposed Action 33:** Already during the creation phase of the National Action Plan, a checklist with criteria and standards for patient information on rare diseases was developed in Working Group 1 (Information Management) which provide the special framework conditions for creation of patient information on RD is taken into account.

	Proposed Action 34: By publishing the checklist in the journal Evidence, Training and Quality in Health Care, among other things, the implementation of the checklist was promoted, as proposed in measure 34, and a professional discourse was initiated. Based on the criteria developed, the Medical Center for Quality in Medicine (ÄZQ) together with ACHSE eV has created brief information for patients (KiP) on ten selected diseases: adrenoleukodystrophy, 22q11 deletion syndrome, hereditary retinal diseases, Osler's disease, cystic fibrosis, sarcoidosis, Doose syndrome, Ormond's disease, Marfan syndrome, nephrotic syndrome. The KiP are available free of charge on the websites of the German Medical Association, and the National Association of Statutory Health Insurance Physicians and on the ÄZQ portals www.patienten-information.de and www.arztbibliothek.de as well as on www.achseonline.de and on Orphanet available. Two more KiPs are being planned. A method report was created by the ÄZQ on the KiP; can be found at www.patienten-information.de. **Proposed Action 35:** In the area of information for patients and medical professionals, the challenges lie in particular in making the developed instruments and offers known to the target groups. Measure proposal 35, the development of a format for good German-language patient information, can make a contribution to the checklist with criteria and standards for patient information on RD. So far there has been no new format development, but rather the gradual improvement of patient information in the course of the implementation of measure proposal 38. ***Area:*** ▪ Joint Communications on the Subject of Rare Diseases **Proposed Action 36:** For the ZIPSE and se-atlas offerings, the NAMSE office can use the existing communication channels via the NAMSE alliance partners and other stakeholders (for example, AG Centers for Rare Diseases) to inform the public about ZIPSE and se-atlas (See proposed measures 36 and 46). For measure proposal 36, a concept for the participation of all NAMSE partners in public relations was developed by ACHSE eV together with the NAMSE office on Rare Disease Day. ***Area:*** ▪ Central Information Portal **Proposed Action 37:** The ZIPSE project (Central Information Portal for Rare Diseases, www.portal- se.de) initiated by the Federal Ministry of Health. The information portal should not contain any primary information, but should instead reference quality-assured information sources that already exist and are being developed (measure proposal 37). As part of the considerations as to how quality assurance of the integrated information pages can be carried out, the checklist with criteria and standards for patient information on RD could be used by integrating the criteria into a self-disclosure form for interested information providers. **Proposed Action 38:** From March 1, 2015 to December 31, 2016, ACHSE eV is carrying out a project with the support of the BKK health insurance company to transfer the disease descriptions from www.achse.info to Orphanet (measure proposal 38). As part of this, the quality criteria will also be made known to member organizations and interlocutors again, updates of the disease descriptions will be encouraged by member organizations and some core criteria will be checked before publication. The operation of www.achse.info has been discontinued.

	Proposed Action 39: As part of the ZIPSE project, an evaluation of the benefits and costs of an information hotline about rare diseases was also carried out. On Rare Disease Day on February 28, 2015, the se-atlas, Medical Care Atlas for Rare Diseases, went online. On the website www.se-atlas.de, those affected, relatives and doctors, but also nonmedical staff and for people with rare diseases in Germany. Recommendations from self-help organizations, collections from ACHSE eV and Orphanet Germany as well as verified self-nominations serve as data sources. Currently (as of March 2017) there are 775 care facilities, 1,350 care offers and 352 self-help organizations registered in the se-atlas. ***Area:*** ▪ Medical and Dental Training and Continued Education **Proposed Action 40:** As a guide for medical and dental faculties for designing curricula and examination content, the National Competency-Based Learning Objectives Catalog for Medicine (NKLM) and Dentistry (NKLZ) was adopted on June 4, 2015 at the general meeting of the 76th Ordinary Medical Faculty Day. The NKML was founded by the Medical Faculty Association together with the Society for Medical Education with the participation of representatives from medical societies and medical students, self-employed organizations, administration, responsible ministries and authorities as well as scientific organizations. Using the criterion of transferability, rare diseases were also included in the list as examples of this group, which consists of more than 7,000 known diseases. When teaching the necessary skills in dealing with rare diseases, the focus is on methodical access to specific information sources and techniques and not so much on detailed knowledge about the rare diseases contained in the NKLM. **Proposed Action 41:** Depending on the demands in the NKLM, proposed measure 41 proposes to anchor general knowledge about rare diseases in the curricula of medical and dental studies. The implementation of this measure has been initiated. Based on the NKLM/NKLZ, the joint project "Competence-oriented learning, teaching and testing in medicine" is a model for the systematic implementation of competency orientation in curricula and examinations at the medical faculties in Baden-Württemberg. It is planned to make the findings and experiences from the model project accessible to other federal states. **Proposed Action 42:** In order to increase medical students' involvement with the topic of RD, contact was made with the Institute for Medical and Pharmaceutical Examination Questions (IMPP). ACHSE eV has developed project ideas for implementation, but financing for implementation has not yet been found. It will then be necessary to examine whether and in what form, in accordance with the goal formulated in proposed measure 42, questions about RD can be included in the IMPP question pool. **Proposed Action 43:** In order to increase the knowledge and special features of RD among primary care providers, NAMSE recommends increasing the imparting of knowledge about RD as part of further medical and dental training. The German Medical Association has earmarked the topic "Dealing with RD" for the revision of the "General content of further training for sections B and C" as part of the amendment to the model further training regulations. Since the entire (sample) further training is currently being revised and this is associated with a very extensive coordination process, implementation is expected in the medium term. For dentistry, an examination is currently underway to determine how basic information on RD can be included in the model continuing education regulations (measure proposal 43). **Proposed Action 44:** From NAMSE's point of view, RD should also be regularly discussed in the area of medical and dental training. It is planned that Type A centres and Type B centres will offer further training events recognized by the State Medical Association at regular

intervals, including patient self-help (measure proposal 44). This measure is therefore dependent on the establishment of the three-tier centre model (see proposed measure 1).

Proposed Action 45: In addition, existing training events organized by patient associations for other rare diseases should be further developed (measure proposal 45). In order to increase medical students' involvement with the topic of RD, contact was made with the IMPP. ACHSE eV has developed project ideas for implementation, but financing for implementation has not yet been found. The Baden-Württemberg State Medical Association has had the University of Tübingen develop an interactive training program on the simulation and e-learning platform INMEDEA. In a model project, virtual patients with RD can be processed interactively and training points can be acquired. With this offer, the State Medical Association would like to contribute to improving the detection and treatment of RD. The measures described are aimed at medical/dental staff.

Area:
- Public Relations

Proposed Action 46: A distinction must be made at this point between public relations work to raise awareness of the topic of RD on the one hand (measure proposal 36) as well as the functioning of the NAMSE and the implementation of the National Action Plan on the other hand (measure proposal 46). The basic premise is that the joint public relations work is managed decentrally via the alliance partners.

The central contact for the alliance partners and other actors is the NAMSE office. This is increasingly answering inquiries from those affected, interested organizations and the press and supports the alliance partners in their public relations work by presenting the progress in specific measures and projects. She also coordinates NAMSE's participation in high-profile events (congresses, meetings). On Rare Disease Day, the office cooperates with ACHSE to offer alliance partners various opportunities to participate in Rare Disease Day. Other tasks carried out by the office as part of public relations work include collecting, processing and disseminating information and providing and providing contact persons.

In addition to public relations work on rare diseases, the proposed measures mentioned in Information for patients and medical professionals, in particular the ZIPSE project and patient information, should be mentioned. The ZIPSE project makes it possible to provide target group-specific information for those affected and their relatives as well as medical, therapeutic and nursing service providers and to place topic-specific, new information and messages. As part of their public relations work, the NAMSE alliance partners can help to make the portal known and make relevant information available to the portal operators in a timely manner.

Area:
- Telemedicine

Proposed Action 47: A survey was carried out among NAMSE's alliance partners about existing offers. In addition, various online platforms (including Atlas Telemedicine) were scanned for telemedicine projects at RD. Contact was made with the Society for Insurance Science and Design eV (GVG). Both in the exchange with the GVG and by reviewing existing projects, it became clear that there are numerous individual initiatives whose instruments are difficult to transfer. One problem is, among other things, that there is insufficient data on the evidence of telemedicine services at the national level. The BMG has responded to the initial situation and developed a catalogue of criteria to support the targeted planning, implementation and evaluation of telemedicine projects. The catalogue presents a

	variety of criteria that must be taken into account when planning telemedicine projects, including in the area of RD. Based on the catalogue of criteria, funds from structural funding could be used specifically to initiate projects. The NAMSE office can help inform institutions about tenders and current developments. In order to develop scenarios in which telemedicine offers can provide valuable support for care and thus describe the role of telemedicine in the area of RD, as proposed in measure 47, the establishment of the centre model is also an essential prerequisite (cf. Proposed measure 1). **Cross-sectional Action Field: Patient Orientation** ***Area:*** ▪ Research **Proposed Action 48:** In order to adequately incorporate the experiences of self-help in the development and implementation of research and care projects for RD, the research-promoting organizations have included information in various information sheets for applications. The BMBF also involves a self-help observer in the assessment of rare disease associations. There is also a greater emphasis on the involvement of patient organizations in research projects in the current E-Rare announcement as well as cooperation with EURORDIS to strengthen participation in E-Rare-3 (measure proposal 48). ***Area:*** ▪ Expert Opinions by the Medical Advisory Service of the German Statutory Health Insurance **Proposed Action 49:** The dialogue between the Medical Service of the National Association of Statutory Health Insurance Funds, the GKV-SV and ACHSE, which began in 2015, was continued in January 2016 with another discussion involving representatives of the Medical Services (MDK). On the basis of a survey carried out by ACHSE among its members, specific problems in connection with the assessment of people with rare diseases were discussed in detail. In the dialogue, in which the relevant socio-medical expert groups from the MDK community were involved, a common understanding was developed on key points and sensitivity to the special concerns of people with rare diseases was improved (measure proposal 49). ***Area:*** ▪ Support and Qualification of Patient Organizations **Proposed Action 50:** the appropriate promotion of the supporting work of self-help, will be implemented by the NAMSE actors as part of ongoing project funding. Due to a new legal regulation in Section 20h SGB V, funding from statutory health insurance companies totalling 74 million euros will be available from 2016 to support health related self-help groups, self-help organizations and self-help contact points. These funds also benefit the RD self-help structures. ▪ European Networks **Proposed Action 51:** The aim of measure proposal 51 is to network the self-help of people with RD to intensify at the international level. The BMG and ACHSE eV support this project ben in their role as members of the EU Commission's expert group for RD. **Action Field 5: Implementation and Future Development**

	Proposed Action 52: At a meeting of the NAMSE steering group in November 2014, it was confirmed that the continuation of the NAMSE in its structure as an alliance is important and that the NAMSE must be institutionalized together with the office. For this purpose, a working group "Legal form and financing of NAMSE" was initiated. This has developed an organizational concept that The alliance is to be transferred into a foundation. A preliminary question about the possible participation of the organizations in NAMSE as a foundation and about the possibilities of financial participation in the future organizational form was carried out by the office. Feedback has been received from around half of the alliance partners, although financial participation is only conceivable for a smaller proportion. The efforts and feedback from the organizations so far show that more time is needed to develop a sustainable structure. With the aim of obtaining impulses for the future content and structure of the NAMSE, a future workshop took place in Berlin on September 20, 2016 with the participation of numerous experts from the field of rare diseases. At NAMSE, a working group is currently dealing with the fundamental issues in connection with the development of an association model and the design of statutes.
Governance and organisational structures	*See main report.*
Funding model	*See main report. Also see implementation actions for progress related to associate actions.*
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	*See main report. Also see implementation actions for progress related to associate actions.*
Personalised medicine, genomics, genetic counselling	*See main report. Also see implementation actions for progress related to associate actions.*
Models of care/care pathways	*See main report. Also see implementation actions for progress related to associate actions.*
Workforce	*See main report. Also see implementation actions for progress related to associate actions.*
European Reference Networks	*See main report. Also see implementation actions for progress related to associate actions.*
EU alignment and participation	*See main report. Also see implementation actions for progress related to associate actions.*
Health information (including rare disease registries)	*See main report. Also see implementation actions for progress related to associate actions.*

Orphan medicines	*See main report. Also see implementation actions for progress related to associate actions.*
Rare disease research	*See main report. Also see implementation actions for progress related to associate actions.*
Alignment beyond the healthcare sector	*See main report. Also see implementation actions for progress related to associate actions.*
Any additional information (for example, background to the strategy or strategy development)	*See main report.*

Key: ACHSE e.V.: Alliance for Chronic Rare Diseases; ÄZQ: Medical Center for Quality in Medicine; BMBF: German Federal Ministry for Education and Research; BMG: the German Federal Ministry of Health; DIMDI: German Institute for Medical Documentation and Information; DFG: German Research Foundation; DKG: German Hospital Federation; EBM: German Uniform Evaluation Standard; ELSA: ethical, legal and social aspects; ERN: European Reference Network; GKV-Spitzenverband; Federal Association of Statutory Health Insurance Funds; GVG: Society for Insurance Science and Design; IMPP: Institute for Medical and Pharmaceutical Examination Questions; IRDIRC: International Rare Diseases Research Consortium; MDK: Medical Services; NAMSE: National Action League for People with Rare Diseases; NGS: next generation sequencing; NKLM: National Competency-Based Learning Objectives Catalog for Medicine; NKLZ: National Competency-Based Learning Objectives Catalog for Dentistry; OSSE: open source register system for RD; RD: Rare Disease; VUD: Association of University Clinics in Germany.
Note: The information in this table was extracted from a version of the original document translated to English using Google Translate.

Table B15. Data extracted for Ireland (National Rare Disease Plan)

Ireland	Strategy information
Author(s) **Title**	Department of Health National Rare Disease Plan for Ireland 2014 – 2018[19]
Timeline	2014-2018
Overall aim(s)	**Vision** An Ireland where – ▪ People with rare disease receive timely access to the best possible evidence-based, patient-centred and family-centred screening (as appropriate), diagnosis, treatment and care through all stages of their lives. ▪ The needs and experiences of people with rare disease are recognised, understood and addressed within all aspects of the Irish health system, including policy, services and research/information systems.
Themes and or priorities	**Principles** Five guiding principles are proposed for Ireland's National Rare Disease Plan. These are intended to guide the implementation and monitoring of the plan in the longer term. It is intended that the principles assist in ensuring that the execution of policy actions remains rooted in what is known to matter to rare disease patients and carers, and also in what is known to be effective in delivering effective change. These principles are: ▪ Equity: Patients resident in Ireland should receive the best possible evidence-based diagnosis and care irrespective of the rarity of their condition and the location of optimal care services. Equality in accordance with prevailing health and other legislation should underpin the provision of care. ▪ Collaboration: Cross-sectoral, cross-border and international cooperation are integral for Ireland to deliver on the vision for rare disease patients and a core activity of all policy actions. ▪ Family-centeredness: Implementation of policy actions should be built around the development of coordinated packages of care for patients and their carers. ▪ Sustainability: A strategic approach to improving the situation of rare disease patients and carers should be sustainable. Policy actions should be implemented in a way that planning, delivering and monitoring rare disease issues become core work of the health system. ▪ Transparency: Progress with the implementation of the policy actions should be transparent to all stakeholders. **Chapter titles:** *(Recommendations grouped under each, except for 'Why a plan is needed' and 'How the National Rare Disease Plan was developed')* ▪ Why a plan is needed ▪ How the National Rare Disease Plan was developed ▪ Recognition of rare disease – Information and research ▪ Prevention, diagnosis and care ▪ Enhancing access to appropriate drugs and technologies ▪ Empowering, protecting and supporting rare disease patients and carers ▪ Implementation, monitoring and review of the National Rare Disease Plan.

Targets (if specified) and measurement method(s) (where available)	*Not mentioned.*
Implementation action(s), lead(s) and key performance indicator(s)	…it is envisaged that the National Rare Disease Plan will be implemented on the basis of the recommendations set out in the report, supported by high-level outcomes underpinned by a series of key outputs/action areas with designated lead agencies. The Steering Group recommends: **Recognition of rare diseases – Information and research** 1. Guidelines be developed on coding and recording of rare diseases within relevant Irish health data systems that are consistent at European and global level. The Health Information and Quality Authority (HIQA) will have a role in this, given its functions regarding information standards, including coding standards. 2. The publication of the Health Identifier Bill and the forthcoming Health Information Bill. 3. The Department of Health and the Health Service Executive (HSE) put in place over 5 years a coherent system to conduct broad epidemiological surveillance of rare disease in Ireland. This epidemiological surveillance should include profiling of rare diseases among high-risk cultural and ethnic minority groups for the purposes of appropriate neonatal screening and improving diagnosis and outcomes. 4. A periodic national report on the epidemiology of rare diseases in Ireland be published by the Department of Health, similar to that prepared for the European EUROPLAN report, and that reporting on rare diseases be integrated into the existing HSE reporting on health and disability services. 5. All existing databases to be mobilised. Systems be put in place to enhance the utility of data held in relevant health service-based information systems, including hospital record, laboratory cytogenetic and molecular genetics data. 6. Irish data on Orphanet be reviewed and a plan for its development agreed, including an assessment of its relocation to an Irish centre if appropriate. This function should be supported by a National Office for Rare Diseases *(further information on the role of this proposed new office is provided in Chapter 4).* 7. Appropriate support be given for the ongoing involvement of Irish registries in relevant European collaborations, including the Surveillance of Rare Cancers in Europe (RARECARE) and European network of population-based registries for the epidemiological surveillance of congenital anomalies (EUROCAT) registries. 8. An All-Ireland Network of Rare Disease Registries, covering the island of Ireland, be developed and that this network work towards enhancing and standardising rare disease registries in line with HIQA draft guidelines, data protection legislation and international best practice. This function should be supported by the new National Office for Rare Diseases. 9. The development of any future information systems provide for a rare disease code in a patient's record in order that all people with rare diseases may be easily identified. The development of a Rare Disease ID Card that could be linked to a person's Personal Public Service Number should also be explored once the provisions of the proposed Information Bill have been enacted and promulgated. 10. A rare disease research network be developed to: a. enhance the quality and relevance of rare disease research on the island of Ireland in a strategic manner in line with the priorities of this National Rare Disease Plan; b. support the integration of rare disease research within relevant forthcoming Government research policy and legislation; c. develop a clearly identifiable online presence, which would act to attract international interest and research partnerships; d. actively pursue potential international research partners;

	e. signpost new and established researchers to relevant resources and contacts; f. facilitate greater international collaboration with relevant registries, organisations and consortia, including the International Rare Disease Research Consortium; g. make proposals to the Department of Health with regard to Irish involvement in international networks such as E-Rare and engage in the rare diseases aspects of the European research infrastructure for biobanking (BBMRI-ERIC), the European Clinical Research Infrastructure Network (ECRIN-ERIC) and other EU infrastructures. 11. Research on rare disease in Ireland adhere to the EURORDIS guiding principles for conducting rare disease research. 12. The role of the designated Centres of Expertise in Ireland should include research relevant to rare disease, in particular with regard to registries, health service and translational research. 13. Ireland becomes a member of ECRIN-ERIC in due course and that the capacity of Ireland's five clinical research facilities to engage in rare disease research nationally or in collaboration with international collaborative research be enhanced. 14. The potential for industry collaboration in research relevant to rare diseases is explored, particularly with regard to research relevant to the diagnosis, treatment and management of rare disease. 15. The forthcoming national biobanking plan provides national coordination and quality standards for biobanking and embraces all opportunities for rare disease research and Ireland becomes a full member of BBMRI-ERIC when the national coordination of biobanking has been established. **Prevention, Diagnosis and Care** 16. With respect to pregnancy: a. Where family members are known to be at risk of being carriers of genes for rare diseases, they have appropriate access to pre-conception genetic testing and counselling, which can inform them about the risks involved in becoming pregnant; b. Making evidence-based, high-quality pre-conceptual care available to women at higher risk of having babies with rare congenital anomalies (for example, women with diabetes or epilepsy); c. Women are supported regarding preparation for a healthy pregnancy, including healthy diets and lifestyles, folic acid supplementation and good maternal antenatal care, which can have a role in the prevention of a small number of rare conditions. 17. The HSE Governance Committee/Group on Newborn Screening within the Integrated Services Directorate be expanded to include a patients' advocate. The Committee should consider the population benefits of newborn screening, including whether programmes need to be expanded or modified, and the need for carrier screening. The Department of Health should also provide a policy framework for population-based screening programmes. 18. The Department of Health consider addressing the need for a review of legislation that indirectly impinges on the Newborn Bloodspot Screening Programme. 19. Governance arrangements for 'send out' genetic tests be strengthened. This should include clinical guidelines for 'send out' tests and yearly audits of the quality and diagnostic yield of tests sent out from non-hospital sources in order to minimise wastage. A national funding perspective is required to maximise quality and cost-efficiency. Centres involved in testing should develop and use guidelines regarding the most commonly tested conditions. 20. The National Clinical Programme for Rare Disease through a National Office for Rare Diseases develop the clinical and organisational governance framework that will underpin care pathways and access to treatment for rare disease patients, particularly in the context of the transition from paediatric care to adult care. 21. National Centres of Expertise (CoEs) in Ireland be identified for groupings of rare conditions, based on clinical need and built on foundations already established. There is an urgent requirement for the HSE to map out CoEs and healthcare pathways, and to

	acknowledge the different role and competencies of CoEs and centres providing care at local level, such mapping to be aligned with the re-organisation of Irish hospitals into hospital groupings. It is also important that broader clinical guidelines take account of the requirements of rare diseases. The potential for cooperation on an all-Ireland basis should be realised. The designation of CoEs should be in accordance with the European Union Committee of Experts on Rare Diseases (EUCERD) quality criteria for CoEs. 22. The HSE integrate CoEs into national funding planning, with provision for adequate staffing for multidisciplinary care, as well as sustainable research infrastructure for clinical investigation in addition to competitive research. 23. The Department of Health and the Health Service Executive (HSE) encourage and support the national Centres of Expertise (when so designated) to seek recognition as EU designated Centres of Expertise or associated national centres in European Reference Networks for Rare Diseases (RD ERNs) according to the timeframe, framework and standards currently being developed at European level through the complementary work of EUCERD and the EU Cross-Border Healthcare Directive 2011/24/EU. 24. Residential respite care be available for children with rare diseases. 25. With respect to palliative care: a. access is provided to appropriate palliative care for people with rare life-limiting conditions; b. guidelines are developed in palliative care provision to address the complex and multisystemic nature of many rare life-limiting conditions; c. the National Development Committee for Children's Palliative Care, chaired by the HSE, take account of the particular needs of children with rare disease in its ongoing programme of work; d. the next National Cancer Strategy could elaborate further on how best to manage rare cancers, especially in the context of this National Rare Disease Plan, where there is a shared objective to detect and treat early patients with rare cancers. 26. Appropriate modules relating to rare disease feature within all undergraduate and postgraduate programmes of both medical professional and carer disciplines. In addition to developing competency requirements and training programmes for medical professionals and carers engaged with rare conditions, practical experience and exposure to patients with rare conditions is advantageous. 27. A system of training in rare diseases for healthcare professionals be addressed through their professional bodies with the support of all stakeholder groups, including patients and their families. Action in this area should build on initiatives already underway or in progress (as outlined in Recommendation 26). 28. The establishment of a National Clinical Programme for Rare Diseases. A key role for this clinical programme will be the mapping, development and implementation of care pathways for rare diseases. 29. The establishment of a National Office for Rare Diseases to facilitate the coordination and timely access to Centres of Expertise nationally and internationally, and to provide up-to-date information regarding new treatments and management options, including clinical trials. **Enhancing access to appropriate drugs and technologies** 30. The HSE develop a Working Group to bring forward appropriate decision criteria for the reimbursement of orphan medicines and technologies. The approach should include an assessment system similar to that for cancer therapies established under the National Cancer Control Programme and link with the Project on the added value of orphan drugs (measured in the daily practice) CAVOMP (Clinical Added Value of Orphan Medicinal Products) at European level. 31. The HSE undertake a preliminary economic evaluation of current activity and costs for orphan medicine and technologies for rare disease patients across all hospitals settings.

	32. Applications for the use of orphan medicines and technologies in hospitals be dealt with in the context of a national budget, rather than through individual hospital budgets, and that the HSE take account of this. 33. The HSE develop a publicly available annual report documenting the use of both existing and new-to-market orphan medicines and technologies in Ireland and a summary of applications received and decisions relating to those applications. 34. The existing horizon scanning between pharmaceutical companies and the HSE, including clinical value assessment authorities, continue and be enhanced so as to improve information available regarding orphan medicines in the pipeline and the future needs for these medicines. 35. The capacity to prescribe all orphan medicines and technologies for ultra-rare conditions be limited to specialist teams designated through the Centres of Expertise. 36. The HSE apply a set of guidelines on the prescribing of orphan medicines and technologies in Ireland. The HSE should evaluate clinical outcomes regarding use of orphan medicines. 37. Clinicians should provide data necessary to the monitoring of prescription patterns and pharmacovigilance, so as to ensure patients' safety and high-quality healthcare. 38. Early dialogue between the HSE and companies who are running clinical trials in Ireland with Irish patients where license approval is imminent. 39. Sponsors could be offered an incentive to run trials in Ireland increasing access to innovation for Irish patients. **Empowering, protecting and supporting rare disease patients and carers** 40. The principles of patients' empowerment be integral to all aspects of this National Rare Disease Plan for Ireland, both now and in the future, in recognition of the fact that patients and their carers require significant clinical and non-clinical support. 41. Arrangements be put in place to support the integration of the experience and expertise of rare disease patients' organisations in the implementation and review of this first National Rare Disease Plan for Ireland. 42. Patients' rights to appropriate assessment and treatment be realised through a recognised national Centre of Expertise or by linkage through the patient's healthcare provider to recognised European Reference Networks (ERNs) and in the context of the EU Cross-Border Healthcare Directive 2011/24/EU. 43. The proposed National Office for Rare Diseases provide support and information to patients. 44. The National Rare Disease Plan for Ireland encompass a holistic and person-centred view of the lives of rare disease patients and their families, one that goes beyond healthcare issues. 45. The HSE and non-governmental organisations (NGOs) provide ongoing support for people living with rare diseases and that they cooperate and promote awareness of rare diseases. 46. The HSE and NGOs avail of the opportunity to promote awareness of and information on rare diseases on Rare Disease Day. **Implementation, Monitoring and Review of the National Rare Disease Plan** 47. An Oversight Implementation Group of relevant stakeholders, including patients' groups, led by the HSE be established to oversee and monitor implementation of the National Rare Disease Plan's recommendations and associated key outputs. The HSE will report to the Department of Health using key performance indicators (KPIs) on a periodic basis in accordance with reporting requirements under the National Service Plan. It should be noted that the European Union has mandated EUCERD's KPIs and that Ireland will have to report on these (see Appendix 5). 48. There should be an overall review of the National Rare Disease Plan prior to development of the next plan in 2019.

	Appendix 5: EU EUCERD Indicators to monitor National Rare Disease Plans ***Background indicators (preparation of the plan/strategy)*** 1. Existence of regulations/laws or equivalent official national decisions that support the establishment and development of a Rare Diseases (RD) plan. 2. Existence of a RD advisory committee. 3. Permanent and official patients' representation in plan development, monitoring and assessment. 4. Adoption of the EU RD definition. ***Content indicators*** 5. Existence of a national policy for establishing Centres of Expertise on RD. 6. Number of national and regional Centres of Expertise adhering to the national policy. 7. Participation of national or regional Centres of Expertise in European Reference Networks. ***Information*** 8. Development of/participation in a comprehensive national and/or regional RD information system. 9. Existence of helplines for RD ***Knowledge, classification/coding, registries and research*** 10. Existence of a national policy on RD clinical practice guideline development and implementation. 11. Type of classification/coding used by the healthcare system. 12. Existence of a national policy on registries or data collection on RD. 13. Existence of RD research programmes and/or projects in the country. 14. Participation in European and international research initiatives. ***Therapies*** 15. Number of Orphan Medical Products with a European Union marketing authorisation and available in the country (i.e. priced and reimbursed or directly supplied by the national health system). 16. Existence of a governmental system for compassionate use of medicinal products. ***Social services*** 17. Existence of programmes to support the integration of RD patients in their daily life. ***Financial support indicators (implementation of the plan/strategy)*** 18. Existence of a policy/decision to ensure long-term sustainability of the RD plan/strategy. 19. Amount of public funds allocated to the RD plan/strategy. 20. Specific public funds allocated for RD research. 21. Public funds specifically allocated for RD research actions/projects per year since the plan started.
Governance and organisational structures	***Steering Group and Subgroups*** The Department convened a Steering Group to oversee the development of Ireland's first National Rare Disease Plan. Five subgroups were established to support the Steering Group, each subgroup being chaired by a member of the Steering Group. Subjects covered were research and information, Centres of Expertise, patients' empowerment on orphan drugs and technologies, and communications. Membership of the Steering Group and subgroups is listed in Appendix 1. Each of the subgroups met and discussed the European recommendations and held extended discussions with other key stakeholders. Reports emanating from the subgroups informed the development of both the consultation process and this final report. Steering Group members: ▪ Department of Health x3

	▪ Health Service Executive x2 (medicine and pharmacy) ▪ The Medical Research Charities Group ▪ Irish Platform for Patients' Organisations Science & Industry ▪ Patient Representative, CEO, Saoirse Foundation (Bee for Battens) ▪ Cystic Fibrosis Ireland ▪ Institute of Public Health in Ireland ▪ The Genetics Rare Disorders Organisation ▪ Institute of Public Health in Ireland ▪ Health Research Board x3 ▪ Irish Medicines Board ▪ Department of Health (Secretariat) Subgroups: ▪ Research and Information ▪ Centres of Expertise ▪ Patient Empowerment ▪ Orphan Drugs and Technologies ▪ Communications **Implementation, Monitoring and Review of the National Rare Disease Plan** The service planning mechanism provides an accountability framework with respect to the delivery of health services. Rare disease management programmes should be specified within the HSE Service Plan mechanism.
Funding model	…publication comes at a time of national economic and budgetary challenges, which have been recognised by the Steering Group when developing the plan. The implementation of this National Rare Disease Plan shall therefore be set in the context of re-orienting current resources for the purposes of advancing these recommendations in the health service, given the prevailing financial constraints. And thus, the present budgetary environment shall be explored to identify and exploit all opportunities for progressing this national plan as the future platform to address the care and treatment of people with rare diseases.
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	*See recommendations 17 and 18.* **Strengths of current National Newborn Screening Programme** ▪ The clinical outcomes of the current National Newborn Screening Programme in Ireland are continually audited and are exemplary as evidenced by international peer review. ▪ The laboratory services are accredited by CPA (UK) to ISO 15189 standards and the laboratory participates in a range of external quality assurance programmes, including Quality Assurance in Laboratory Testing for Inborn Errors of Metabolism, UK Expert Quality Assessment Services and Region-4- Genetics Collaboration (Mayo Clinic, National Institutes of Health). ▪ The programme is monitored by its Clinical Director, who reports to the National Newborn Bloodspot Screening Governance Group.

	▪ The programme for the existing conditions meets the targets in the Executive Agency for Health and Consumers 2011 report, for example, on expectancy for sample delivery, numbers and turnaround times. **Weaknesses of current National Newborn Screening Programme** ▪ Newborn screening is an essential public health responsibility, not currently mandated by law and lacking the appropriate legislative framework in Ireland. ▪ There is no health economics evaluation of newborn screening. ▪ There is a lack of patients' advocacy groups, in particular for newborns, and a lack of public understanding of the merits and public health consequences of appropriate newborn screening for the Irish population. ▪ Difficult economic conditions and a health system under reform and re-organisation present considerable challenges to the Newborn Screening Programme.
Personalised medicine, genomics, genetic counselling	*See recommendations 16 and 19.* **Strengths of the current genetic testing system** ▪ Testing done through the National Centre for Medical Genetics (NCMG) meets international standards. ▪ The Disability Act Part IV, passed by the Oireachtas and signed into law in 2005, states that genetic testing shall not be carried out unless the consent of the person has been obtained. In addition, genetic tests cannot be used in relation to employment, insurance, pensions or mortgages. **Weaknesses of the current genetic testing system** ▪ A report submitted in late 2012 to Clinical Leads in Paediatrics indicates a waiting time of 12-24 months for referral to NCMG. Due to funding challenges and unfavourable consultant: patient ratios, there is lack of an appropriate method of tracking patients without an appropriate database or specific disease registries. ▪ Difficulties have arisen in the last two years with funding challenges and excessive untimely access to appointments according to required standards. This has resulted, inter alia, in non-accredited providers sending tests out without referring to specialists in the area or to standard guidelines, giving rise to cost-inefficiencies and risk issues. ▪ The model of funding is on a local model basis. NCMG do not have a ring-fenced budget. Long waiting times impact on, for example, immediate access for linked programmes such as the National Centre for Inherited Metabolic Disorders. ▪ In addition to delays in diagnosis that may arise from resource challenges in established testing programmes, for ultra-rare diseases, the very rarity of the condition in a relatively small population such as Ireland poses particular diagnostic challenges. This is due to lack of knowledge among General Practitioners (GPs), other health professionals and parents about the signs and symptoms and the appropriate treatment pathways. Many patients and families affected have an undesirably long wait for a correct diagnosis and a worrying number receive an incorrect diagnosis before their final diagnosis is made. However, more recently the NCMG has developed a University College Dublin-linked microsite which provides practical advice to community practitioners regarding testing and the referral process in general for genetic rare diseases. **Protecting patients' rights** Rapid advances in genetic knowledge create special legal and ethical issues, including informed consent concerning genetic testing and genetic research; confidentiality and the duty to inform those potentially affected by genetic-related conditions; liability and risk management to avoid malpractice; privacy interests concerning identifiable genetic data; ethical analysis of public health initiatives (genetic screening, national registries); insurance and employment discrimination; sex selection; and genetic and intellectual property issues.

Models of care/care pathways	*See recommendations 20, 21, 22, 23, 24, 25, 28, 29, 42, 43, 44, and 45.* Due to the complexity of the various rare conditions and to provide efficient formal guidance and support to care coordinators, it is recommended that a rare disease care pathway be developed. This would provide for high-quality care and would assist in guiding patients through care and social services, increase efficiency of State resources and reduce waiting times for accessing support and social services. It is recommended that this pathway should: 1. Identify appropriate consultants and medical care professionals and support centres. 2. Provide information, educational and social entitlements appropriate to the condition, including, among others: ▪ Medical/GP card; ▪ Long-term Illness card; ▪ Carer's Benefit/Allowance; ▪ Domiciliary Allowance; ▪ educational grants and support services; ▪ Disability benefits, including housing adoption grants, disability driver/passenger benefits; ▪ contact details for counselling and psychological services. 3. Where standards of international best practice exist for the care of a person with a rare disease, these should be implemented. If no international standard is available, a template needs to be created. The template should outline the treatments, therapies and required specialists as standard. It should also take account of guidance developed by the European Reference Networks. In addition, the care pathway should also include oral/dental health needs, particularly in the paediatric dentistry domain. 4. The transition from paediatric care to adult care needs to be managed effectively and seamlessly. At present, transition for those with rare conditions occurs on an *ad hoc* basis, with resultant stress, fear and worry for patients and families. At this highly sensitive time, teenage patients and their families need additional support. This should be coordinated centrally by a lead professional throughout the process. Guidelines for this process are required for both patients and staff. Protocols and associated training for staff are also essential to ensure that this support is accessible to all patients with rare diseases.
Workforce	*See recommendations 26 and 27.* **Treatment and care** ***Strengths of current system*** ▪ Well-trained medical and paramedical staff. ▪ Commitment of relevant staff to provide a quality service. ▪ Good linkages and cooperation with international colleagues and European Reference Networks (ERNs). ***Weaknesses of current system*** ▪ Challenges around staffing levels and lack of recognition of some of the main reference centres. ▪ Lack of ring-fenced budgets and national funding. No health economics evaluations apparently ever performed to illustrate predicted cost savings (for example, for newborn screening) of treating rare diseases. ▪ Lack of understanding and education of the public at large in rare diseases, including local managers given responsibility for funding. ▪ Lack of protected time for staff in this area and unfavourable patient: physician ratios. ▪ Lack of funded programme for trainees in this area and HSE embargo on recruitment eliminates trainee opportunities to facilitate shared care at community level and make cost-efficiencies.

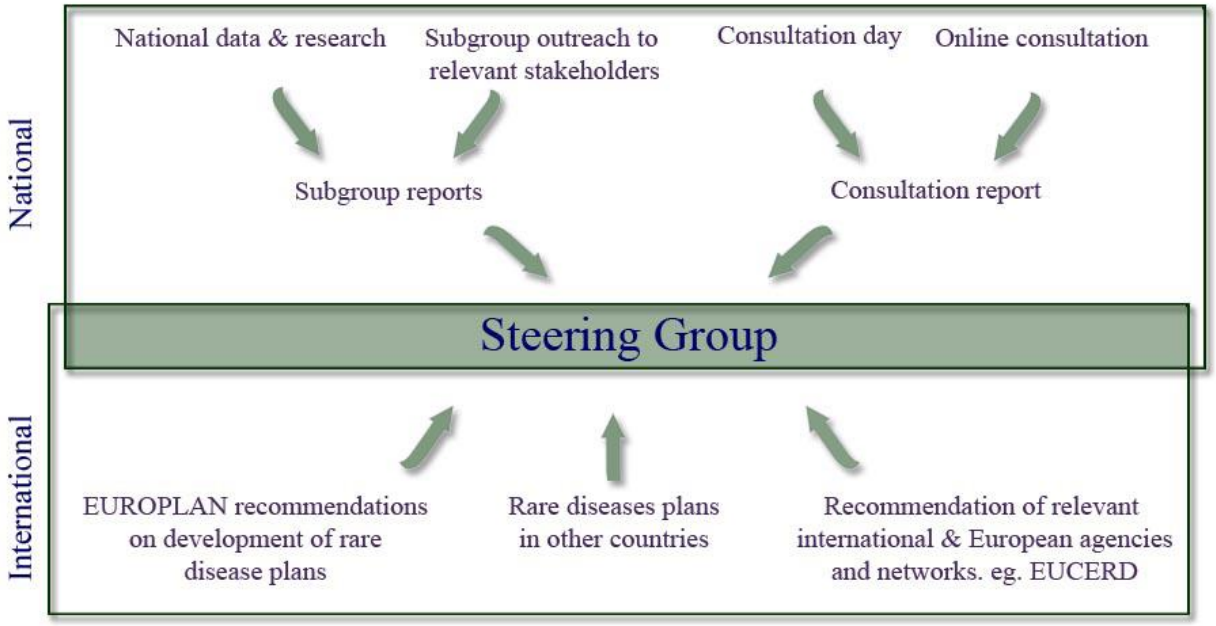
European Reference Networks	*See recommendations 21, 22, 23, and 42.* While healthcare pathways may be well defined in Ireland for some rare disorders (for example, hereditary coagulation disorders), through well-established CoEs, for many conditions and for ultra-rare disorders, there may not be sufficient local expertise in Ireland. For such situations, the development and use of European Reference Networks (ERNs) is particularly relevant. Ireland participates, or has participated, in the following Pilot European Reference Networks for rare diseases: Dyscerne, European network on centre of reference on porphyria, European Reference Network for rare and complex epilepsies, European Reference Network for the thematic grouping of rare neuromuscular diseases, rare bleeding disorders and the Paediatric Hodgkin Lymphoma Network. At the Irish EUROPLAN Conference 2011, it was agreed that strong collaboration exists in this area among the scientific communities and the patients' groups with European groups. There is some participation among clinicians in pilot ERNs, but this is not well coordinated and is better in some disease areas than others. ERNs can improve knowledge by sharing and creating mutual databases and registries of information and resources. This can increase cohorts for research studies and clinical trials, and develop standards of care for national CoEs.
EU alignment and participation	*See recommendations 6, 7, 11, 13, 30, 42, and 47.* **Treatment and care** ***Strengths of current system*** ▪ Good linkages and cooperation with international colleagues and ERNs. ***Weaknesses of current system*** ▪ No linkage of databases, no registries and lack of central office to coordinate activities, such as contact point for Orphanet according to its standard operating procedure. ▪ No research infrastructure funding provided for essential core activities of Centres of Expertise, such as management of databases, registries, outcome studies.
Health information (including rare disease registries)	*See recommendations 1, 2, 3, 4, 5, 6, 7, 8, and 9.* **Strengths and weaknesses of information on rare diseases in Ireland** The Research and Information Subgroup of the Steering Committee were tasked with identifying the strengths and weaknesses of the current system of information on rare diseases in Ireland. An overview of its findings, together with key findings from the consultation process, is provided below. ***Strengths of the current system*** ▪ National Cancer Registry and linkages on RARECARE project. ▪ A small number of high functioning Irish rare disease registries. ▪ Department of Health commitment to the Health Information Bill and the need to adopt a universal patient identifier. ▪ Information collected through the national Newborn Screening Programme. ▪ Irish membership of EUROCAT (a European network of population-based registries for epidemiological surveillance of congenital anomalies) and other European registries. ▪ Membership of Orphanet. ***Weaknesses of the current system*** ▪ Lack of clarity on implications for rare disease information in forthcoming policy and legislation (for example, Health Information Bill, Tissue Act). ▪ No requirement for the Department of Health or any other body to report on national profile of rare disease.

	▪ No system established to collate and analyse available data and report on national profile of rare diseases. ▪ ICD-10 coding system is a blunt instrument for recording rare disease. ▪ Lack of specific health information standards for coding and reporting of rare diseases, prohibiting meaningful identification of rare diseases within national health information systems. ▪ Hospital record data and diagnostic laboratory data underutilised, with lack of capacity in terms of data management systems. ▪ No transparent communication system in place to facilitate translation of rare disease data and evidence into health service policies relating to appropriate workforce planning and commissioning of services. ▪ Lack of overall strategic approach to rare disease registries, with diversity of standards, governance and fragmentation of resources across registries, and with no single rare disease registry in place. ▪ Challenge presented by substantial number of diseases/disorders with no name.
Orphan medicines	*See recommendations 30-39.* **Strengths and weaknesses of access to medicines and technologies** ***Strengths of current system*** ▪ An established system of health technology assessment and assessment for new pharmaceutical agents exists in Ireland. ▪ The existing systems have been successful in supporting the access of rare cancer patients to appropriate orphan medicines and technologies. ▪ The system and practice of early interaction with the National Centre for Pharmacoeconomics has proven helpful in the planning process. ▪ Ireland is considering approaches in which the 'money follows the patient' and this will be of benefit to rare disease patients. ▪ A large pharmaceutical industry and skilled workforce exists in Ireland, which ensures there are pathways for treatments to enter the Irish system. ***Weaknesses of current system*** ▪ There is no ring-fenced fund to support access to orphan medicines and technologies. Current budgetary approaches are fragmented and may perpetuate inequalities in access to orphan medicines and technologies. ▪ Rationalisation of health service resources is required under current economic conditions. The focus on increasing cost-effectiveness at system level can inadvertently disadvantage the needs of individual rare disease patients requiring complex and sometimes costly therapies. There is a need to explore new approaches in the assessment of orphan drugs and technologies that respect the patients' right to treatment, irrespective of the rarity of their disorder. There will always be competing demands for scarce healthcare resources. This highlights the need for rigorous evaluation so that services and treatments achieve an acceptable level of cost-effectiveness and represent value for money and benefits for patients; ▪ Decision-making around orphan medicines can often involve difficult social and ethical considerations since there may be some uncertainty about the exact magnitude of the clinical benefit and proposed prices may be quite high. This can result in protracted price negotiations and potential delays in access. ▪ Adequate and equitable decision-making in terms of availability of some orphan medicines and technologies is hindered by the requirement that the cost of such products be met from within hospital budgets. ▪ Transparency and communication are key themes for patients and their organisations within the processes relevant to the approval, assessment and reimbursement of orphan medicines and technologies. There is no clear system supporting complaints and appeal for decisions made in the context of orphan medicines and technologies in Ireland. ▪ Ireland's potential role in supporting the development of orphan medicines and technologies is underdeveloped at present.

	Appendix 4: Principles relating to assessment for reimbursement of orphan medicines The 10 principles that could describe any new route for assessing pricing and reimbursement of Orphan Medicines are: ▪ Be transparent and accountable. ▪ Support rational decision-making. ▪ Best quality evidence which is available. ▪ Promote accessibility and equity and reflect societal values. ▪ Support improvements to economically efficient or clinically effective service provision. ▪ Realistic predictions of future need. ▪ Demonstrate how the evidence has been considered in a robust and documentable process, able to withstand legal challenge. ▪ Maintain consistency, but allow some flexibility in balancing the relative importance of criteria. ▪ Clear criteria, which should be used as a structure for the evaluation and decision-making process. ▪ Ensure that the criteria and the approach to using them are reviewed regularly to incorporate changes in external context.
Rare disease research	*See recommendations 10, 11, 12, 13, 14, 15 and 22.* **Strengths and weaknesses of rare disease research in Ireland** The Research and Information Subgroup of the Steering Group were tasked with identifying strengths and weaknesses of research on rare diseases in Ireland. An overview of its findings, together with key findings from the consultation process, is provided below. ***Strengths of the current system*** ▪ Rare disease research performing well within Medical Research Charities Group (MRCG)/Health Research Board Joint Funding Scheme. ▪ Some successful models and projects bringing in international funding. ▪ MRCG is a platform for rare disease patients' organisations to become involved in research. ▪ Professional societies, groups and seminars are a forum for sharing of research interests and findings (for example, Irish Society of Human Genetics). ▪ ECRIN/ICRIN involvement in rare disease research and facilitation of multinational clinical trials. ▪ Opportunities for rare disease research presented by ongoing national longitudinal studies and surveys. ***Weaknesses of the current system*** ▪ Like many disease groups, there is no central source of information on rare disease research, such as an office for rare disease, rare disease research platform or designated Centre of Expertise with this role. ▪ Lack of structured, reliable, complete and accessible information systems/registers. ▪ Networking of rare disease researchers occurring on an *ad hoc* basis. ▪ Overall low level of international collaboration. ▪ No overall strategic approach to rare disease research. ▪ Limited supports for clinical specialities relevant to rare diseases conducting research in terms of dedicated staff time, resources and linkages with career development pathways (rare diseases share this issue with other disease areas). ▪ Majority of research focused on 'common' rare diseases rather than 'rare' rare diseases. ▪ Little activity in terms of rare disease research in primary care setting. ▪ Lack of research on broader aspects of rare disease, including education, disability, employment, social services and end-of-life care. **Treatment and care** ***Strengths of current system***

	▪ Very active and committed patients' support groups (for example, Genetics Rare Diseases Organisation, Irish Platform for Patient Organisations, Science and Industry, MRCG). ▪ Good linkages and cooperation with international colleagues and ERNs. ▪ Major opportunities for epidemiological research with population base and high prevalence of genetic recessive disease in Irish population. ▪ Strong Pharma base for collaboration in Ireland. ***Weaknesses of current system*** ▪ No linkage of databases, no registries and lack of central office to coordinate activities, such as contact point for Orphanet according to its standard operating procedure. ▪ No research infrastructure funding provided for essential core activities of Centres of Expertise, such as management of databases, registries, outcome studies. ▪ Lack of protected time for staff in this area and unfavourable patient: physician ratios. ▪ Lack of information technology linkages across hospitals to facilitate data sharing and development of e-medicine.
Alignment beyond the healthcare sector	*See recommendations 40, 41, 44, 45, and 46.* **Protecting patients' rights** The current legislative and policy environment governing these latter areas (of privacy, confidentiality and consent) offer some protection and coverage to patients with rare diseases; but of course there is always scope for improvements as policy and protection agendas are developed and advanced further in the areas of: ▪ education and support ▪ employment protection ▪ benefit and pension protection. It is essential that discrimination against a person based on their genetic heritage – be it family history of inherited disease or the results of genetic tests – is avoided and properly handled. The principles enshrined in the Convention on Human Rights and Biomedicine, the United Nations (UN) Convention on the Rights of Persons with Disabilities (UN, 2006) and the EU Charter of Fundamental Rights (European Parliament, 2000) are all examples of such international conventions applicable in this context. In recognition of the challenges facing patients and their families with rare diseases, it is important that health and social benefit programmes are applied in a fair and transparent manner. Rapid advances in genetic knowledge create special legal and ethical issues, including informed consent concerning genetic testing and genetic research; confidentiality and the duty to inform those potentially affected by genetic-related conditions; liability and risk management to avoid malpractice; privacy interests concerning identifiable genetic data; ethical analysis of public health initiatives (genetic screening, national registries); insurance and employment discrimination; sex selection; and genetic and intellectual property issues. **Developing and valuing carers** The Steering Group and its Subgroups consider that bringing the roadmap for implementation contained within the National Carers' Strategy (*National Carers' Strategy – Recognised, Supported, Empowered,* published by the Department of Health in 2011) into reality would be hugely beneficial to carers of rare disease patients, the patients themselves and wider society. However, it is also recognised that carers of rare disease patients differ from the national profile and also that caring in the rare disease context can bring additional challenges. These unique challenges with respect to rare diseases must be taken on board when it comes to the development of further health and social protection measures.

	Delivering holistic packages of care – Rare disease beyond the healthcare setting Recurring themes that emanated from this dimension of the consultation included: ▪ social isolation and exclusion; ▪ adapting to disability; ▪ loss of employment and independence at a young age; ▪ the need for interdisciplinary packages of care that include psychological/counselling services; ▪ a general lack of understanding of rare diseases and their implications outside of the health system in areas such as education, employment and disability.
Any additional information (for example, background to the strategy or strategy development)	**Definition of rare disease** The European definition considers a disease to be rare if it occurs with a prevalence of <5 (5 or less) per 10,000 of the European population (European Parliament and European Council (2000) – EU Legislation Regulation (EC) No. 141/2000 on orphan medicinal products) and this definition is recognised in Ireland. The definition of a rare cancer in Ireland differs from the overall definition used for rare disease. Cancers with an annual *incidence* of less than 6 per 100,000 European population are considered rare. There is currently no European definition of ultra-rare disease. In England and Wales, ultra-rare diseases are considered as those with a prevalence of less than 1 per 50,000 population, equivalent to diseases with less than 1,000 known cases in the region. Adopting a similar definition for Ireland would mean that diseases considered 'ultra-rare' are those for which there are less than 100 confirmed cases in Ireland. **How the National Rare Disease Plan was developed** ***Steering Group and Subgroups*** In January 2011, at a EUROPLAN Conference organised by patients' representative organisations in Ireland, the Department of Health announced its intention to commence work on a rare disease plan for Ireland. *See 'Governance and organisational structures' section for details.* ***Consultation process*** The Department of Health, with the support of the Steering Group and allied subgroups, undertook a strategic consultation process between June and August 2012. Two methods were employed: the holding of a consultation event and the gathering of information through an online survey. The consultation day was launched by Minister James Reilly in Farmleigh on 11th June 2012. A wide range of participants were invited. To complement the findings from this event and ensure a comprehensive and widespread consultation, an online survey was also available to the public for five weeks during June and July. The findings of the consultation process are being published in a separate report, but in the meanwhile, its key findings are highlighted in the relevant chapters throughout this report and they are also reflected in the plan's recommendations. **Figure 1: Key determinants that informed the development of Ireland's first National Rare Disease Plan**



Other determinants of the National Rare Disease Plan

In developing Ireland's first National Rare Disease Plan, the Steering Group was keenly aware of the need to maximise benefits and synergies with other rare disease developments internationally. In particular, as the UK was developing a rare disease plan along within a similar timescale, it was recognised that efforts should be made to realise shared benefits for rare disease patients on the island of Ireland. Thus, members of Ireland's Department of Health met with their counterparts in Northern Ireland to consider these issues. Further ongoing communication will be maintained for the purposes of ensuring an appropriate joint approach on potential areas for collaboration.

It was also recognised that other European countries were further along in the development of rare disease plans. For example, France has published its second rare disease plan, with clear learning from the previous edition. Such experience should inform the Irish planning process (EURORDIS, 2013). The Steering Group, therefore, attempted to ensure that the direction of the Irish plan would have a reasonable fit with the broad direction of plans in other European countries. In addition, efforts were made to integrate elements of European and global best practice as set out by key lead agencies at European level, including EURORDIS and EURCERD.

Key: BBMRI-ERIC: European research infrastructure for biobanking; CoE: National Centres of Expertise; ECRIN-ERIC: European Clinical Research Infrastructure Network; EU: European Union; EUROCAT: European network of population-based registries for the epidemiological surveillance of congenital anomalies; ERN: European Reference Network; EUCERD: the European Union Committee of Experts on Rare Diseases; GP: general practitioner; HIQA: Health Information and Quality Authority; HSE: Health Service Executive; KPI: key performance indicator; MRCG: Medical Research Charities Group; NCMG: National Centre for Medical Genetics; NGO: non-governmental organisations; UN: United Nations; RARECARE: Surveillance of Rare Cancers in Europe; RD: Rare Diseases.

Table B16. Data extracted for Ireland (Interim report)

Ireland	Strategy information
Author(s) **Title**	Department of Health Interim Report on National Rare Disease Plan for Ireland 2014-2018 (Interim Report on Implementation and Summary of Recommendations)[45, 46]
Timeline	2017-2018 (Interim report published on 28 February 2017, National Plan ran from 2014-2018)
Overall aim(s)	*See National Rare Disease Plan for Ireland 2014 – 2018.*
Themes and or priorities	**The National Plan** The report consists of 7 chapters exploring a range of subject matters pertinent to the diagnosis, treatment and care of patients with rare diseases and their carers. A brief summary of each of these areas is as follows: ▪ **Why a plan is needed**: The chapter dedicated to this subject defined rare diseases and estimated the level of these in the Irish population. It set out the background in Ireland and in the European Union context, and included the vision and underlying principles of this first National Rare Disease Plan for Ireland, covering the years 2014-2018. ▪ **How the National Rare Disease Plan was developed**: The report described the national Steering Group that formulated the Rare Disease Plan and how it was developed with key stakeholders. In particular, it referred to the EUROPLAN Conference 2011 that led to the establishment of the Steering Group, the national consultation conference and the online public consultation, all of which played a key role in the development of the plan. A report on the public consultation process was published alongside the National Rare Disease Plan for Ireland. ▪ **Recognition of rare disease – Information and research**: A specific chapter is dedicated to dealing with the recognition of rare diseases and the availability of information and research on them. It began with defining 'a rare disease' and then proceeded to cover pertinent areas on these topics, such as epidemiology, registers and computer information systems, exploring the strengths and weaknesses of each. It went on to examine the research dimension of rare diseases, covering such areas as funding of research in Ireland, networks of researchers, participation in international initiatives and infrastructure. The final section explored the opportunities and challenges in the area. ▪ **Prevention, diagnosis and care**: The report explored issues around the prevention, diagnosis and treatment of rare diseases from an Irish context. Screening services, in the guise of the National Newborn Screening Programme, along with primary prevention measures, received attention at the start of the chapter, with the former assessed for its strengths and weaknesses. Genetic testing services in Ireland were examined as part of the diagnostic element of dealing with rare diseases, followed by treatment and care services available. The context for services for EU patients and the question of improving care and care services, such as respite and palliative care, were also discussed. ▪ **Enhancing access to appropriate drugs and technologies**: The challenges associated with drugs and technologies were examined in the report. It explored the various paths existing for the designation of orphan drugs and technologies, both at European and Irish level; the associated avenues for making these available to patients through community and hospital drug schemes; and accompanying budgets for funding such access. ▪ **Empowering, protecting and supporting rare disease patients and carers**: A chapter in the report provided the opportunity to draw on the issues of rare disease from the perspectives of the patient and the carer. It was about empowering both through various

	means such as protecting their rights, preserving equity and facilitating access to accurate and timely information. The benefits of providing holistic care packages were examined, together with the impetus for developing the effectiveness of patients' organisations. ▪ **Implementation, monitoring and review of the National Rare Disease Plan**: It was acknowledged that the National Rare Disease Plan was being published at a time of significant health reform in the areas of primary care and acute hospital care. The report set out implementation and monitoring arrangements through the service planning process, in addition to planning for the next National Rare Disease Plan in 2019.
Targets (if specified) and measurement method(s) (where available)	*Not mentioned.*
Implementation action(s), lead(s) and key performance indicator(s)	**Summary of Recommendations (Progress to date)** ***Recommendation 1*** The European Union (EU) Commission Expert Group on Rare Diseases recommendation is that member states should consider adding Orpha codes to their country's health information system and explore the feasibility and resources needed to do so. ICD-11 coding is expected to commence in 2018, but it is not yet known to what degree this will enhance recognition of rare diseases. An Electronic Patient Record is being piloted with LauraLynn, a children's palliative care service and other work is being piloted on the Epilepsy Electronic Patient Record System. Orphacodes have been applied on a pilot basis to health information systems in other European countries. An e-Health Strategy was launched in December 2013 and an allied Knowledge and Information Strategy in May 2015. The e-health unit is progressing a number of strategic e-health programmes: Individual Health Identifier (see details under Recommendation 2 below); Electronic Health Record; National Children's Hospital; Primary care IT; Cancer care e-health. An area for Orpha Codes was created within the Proof-Of-Concept (phase 1) of the National Data Dictionary and Data Model. Following review and trialling of it by stakeholders, the business case for a solution was approved and procured by the Health Service Executive (HSE). As the HSE progresses with this, Orpha Code Catalogues will be included in the Data Dictionary as a Health Care Classification Standard along with others like ICD-10, Loinc, SNOMED Ct and so on. Over the coming years the data dictionary will assist in a stepped approach in developing capabilities around terminology, standards and interoperability. The HSE currently uses the Australian Modification of ICD10 (called ICD-10-AM) in its Hospital In-Patient Enquiry system with possible scope of engaging with Orphanet on rare diseases. The EU Commission division Directorate-General for Health and Food Safety (DG SANTE) has now entrusted the EU Joint Research Centre (JRC) with the development and maintenance of the European Platform on Rare Diseases Registration. Its principal goal is to enable sharing and use of rare diseases' patient data across Europe, among the multitude of existing patient's registries within and across the EU. This should facilitate basis and translational research, epidemiological and clinical trials, other studies, along with policy guidance and support. The JRC envisages a number of endpoints of the Platform including generation centres of tools and support to promote interoperability between Rare Disease patients' registries; a registry of European rare diseases registries; and a hub to provide access to European Rare Disease data collections. ***Recommendation 2*** The Health Identifiers Bill was published in 2013 and enacted in 2014. The Individual Health Identifier part of the project is now being implemented by the HSE. A revised and much expanded General Scheme of a Health Information and Patient Safety Bill was approved by the government in November 2015 and published on the Department of Health's website. It is currently with the Attorney-General's Office for formal drafting and with the Oireachtas Committee on Health for Pre-Legislative Scrutiny.

	Recommendation 3 Surveillance of rare diseases in Ireland is somewhat contingent on the development of coding for the recording of each individual rare disease. ICD 11 is being developed and tested; but in the interim, the Commission Expert Group on Rare Diseases has recommended that Orpha codes be considered for use alongside existing health information codes. This therefore refers back to recommendation No 1 above and the work of the HSE in giving consideration to use of orpha codes alongside existing coding infrastructure. A review of data in patient registries in Ireland has been completed by the National Rare Disease Office. ***Recommendation 4*** Progress on this is contingent on tracking rare disease in health information systems. The National Rare Disease Office has now been established and funded by the HSE with funding provided by the EU Commission. In time, it's envisaged that the remit of the office may include assisting with and supporting research and population studies on rare diseases with various public partners. ***Recommendation 5*** The establishment of the National Rare Disease Office will in time, assist with work on this recommendation. This is also linked to the recommendation on coding for rare diseases referred to above. ***Recommendation 6*** The development of data from Ireland on Orphanet is being progressed through the National Rare Disease Office. ▪ A Business Plan was prepared by the Clinical Programme 2014 -2015 to develop this function which was subsequently supported by the HSE. The HSE is a co-applicant on the (June 2016 – May 2019) 3rd EC Rare Diseases Joint Action (beneficiary 16). The Joint Action provides 3 years part (joint) funding for one Orphanet Information Scientist to be housed within the National Rare Disease Office (NRDO). Prof. E Treacy is the country co-ordinator for this function and national Orphanet Validator. ▪ Manchester ceased supporting the Irish arm of their Orphanet operation in September 2014. The Irish Orphanet function was officially launched on June 2015 at the National Rare Diseases Office with the Senior Information Scientist/Project Manager. ▪ Irish Orphanet data is in the process of being verified and expanded, according to Orphanet quality standards and quality assessment review, under the guidance of the Orphanet Ireland Country Coordinator (Prof E Treacy) and the Orphanet International coordination team in Paris. The current position on the creation of a network on genetics and genomic medicine is that: ▪ The establishment of a National Genetic & Genomic Medicine Network (NGGMN) would bring together all parties within the field of genomic medicine ▪ NGGMN should operate on hub and spoke basis with dedicated outreach clinics ▪ The creation of a National Genetic and Genomic Medicine Network would provide a modern integrated genetic medicine service, engaged in patient care, education and translational research. ***Recommendation 7*** The EU Commission through its JRC is also active in the area of rare disease registries. It has begun an exercise of identifying registries referred to in the national plans of member states. The NRDO has performed a preliminary situation analysis of the existing Rare Disease registries this year and is in the process of assigning these known registries on our national orphanet site. The JRC is working towards a European Platform on rare diseases registration. The EU Commission division DG SANTE has now entrusted the EU JRC with the development and maintenance of the European Platform on Rare Diseases Registration. Its principal goal is to enable sharing and use of

	rare diseases' patient data across Europe, among the multitude of existing patient's registries within and across the EU. This should facilitate basis and translational research, epidemiological and clinical trials, other studies, along with policy guidance and support. The JRC envisages a number of endpoints of the Platform including generation centres of tools and support to promote interoperability between RD patients' registries; a registry of European rare diseases registries; and a hub to provide access to European RD data collections. The National Cancer Registry of Ireland continues to be involved in the Surveillance of Rare Cancers in Europe European collaboration. An Irish representative is included on the European Joint Action on Rare Cancers. Ireland remains a partner in the European network of population-based registries for the epidemiological surveillance of congenital anomalies registry. ***Recommendation 8*** The Programme for Government, *A Programme for Partnership Government* provides at paragraph 5.3.23 for the development of National Patient Disease Registries. The Health Information and Patient Safety Bill will support this. A revised and much expanded General Scheme of a Health Information and Patient Safety Bill was approved by the government in November 2015 and published on the Department of Health's website. It is currently with the Attorney-General's Office for formal drafting and with the Oireachtas Committee on Health for Pre-Legislative Scrutiny. The NRDO staff reviewed existing Irish rare disease registries in summer 2015. The Orphanet entries of the 15 active Rare Disease registries in Ireland have been updated. There is no communication between these registries or common data sets in use. It was announced in early 2016 that Northern Ireland is collaborating with the United Kingdom Congenital Anomalies and Rare Disease Registry. As there are an estimated 280,000 Irish citizens with rare diseases, a South of Ireland rare disease registry will require the appropriate commissioning and national funding. Also support from eHealth and implementation of the Unique Patient Identifiers will be required. *See details on JRC under Recommendation 7.* Note that compliance of registries with the Epic-Rare minimal dataset remains unclear. ***Recommendation 9*** The recommendation of the Commission Expert Group on Rare Diseases on member states giving consideration to using Orpha codes alongside existing codes in health information systems is directly applicable here. This refers back to earlier recommendations. Codification of data within the National Rare Disease office for any spreadsheets or databases uses Orphacodes. Preliminary contact has been made by NRDO staff with the eHealth informatics designers regarding the wish to have an Orphacodes box on eHealth forms to provide the necessary data links to Orphanet files regarding correspondence of ICD codes to Orphacodes. ***Recommendation 10*** The Health Research Board (HRB) made 13 awards for rare disease projects in 2014/15. This includes 7 awards jointly with the Medical Research Charities Group (MRCG) partners and 6 awards through HRB only schemes (Health Research Award and HPF). Irish data on Orphanet will benefit from an update in terms of the full scope of rare disease research underway nationally. In November 2014, the Minister for Health announced €850,000 for investment into charity-led research priorities, which particularly benefits rare disease research. Five charities were to provide matching funding bringing total investment to €1.9M. They were to share €850,000 in State funding to take part in international research into rare medical conditions, including respiratory infections and retinal blindness. It is a practical example of collaboration between the State and the charity sector with the intention of benefiting Irish people affected by rare disease. The five charities taking part are Alpha One, Cystinosis Ireland, Fighting Blindness, the Irish Thoracic Society, and the Royal Victoria Eye and Ear Hospital Research Foundation. Only rare diseases that have patient organisations, who are members of the MRCG (and who can afford to fund research) have the potential to access this funding. This funding scheme is not just for rare diseases but for all disease areas represented by MRCG charities. In 2016, the next cohort of projects was funded by the State with €1.686M,

	matched by charity funding of €1.224M. The total funding of €2.91M is shared between 11 charities, including Cystinosis Ireland, Fighting Blindness, Muscular Dystrophy Ireland, Irish Nephrology Society and others. Six of the 15 projects with a total value of €1.1M address rare diseases. The next round of this joint funding initiative will open in autumn 2017. The HRB is funding researchers internationally where no research capacity exists in Ireland, through the Joint Funding Scheme. In addition, a number of Irish-based clinical trials on rare diseases are registered on Orphanet. The information on the full scope of clinical trials is incomplete at present. These have mostly occurred in the context of Cancer Trials Ireland conducting multi-site trials on cancer treatments. In May 2016 a meeting took place between the Department of Health, Genomics Medicine Ireland and the National Treasury Management Agency, at which the Department was advised that an Irish genome sequencing project is to be carried out by Genomics Medicine Ireland. It was advised that this project is to run over three years and will sequence 45,000 genomes. It was also advised that €40m in funding had already been secured for the project as part of the initial investment of €150m required for the project. Some funding of the project will be provided by the National Treasury Management Agency. There is currently a call under from the European Commission Horizon 2020, which relates to - Diagnostic Characterisation of Rare Diseases: Apply genomics and/or other -genomics for molecular characterisation of rare diseases. New Therapies for Rare Diseases: includes appropriate plans to engage with patient organisations; support clinical trials on substances where orphan designation has been given by the European Commission (EC). The HRB submitted a business case to join the European Clinical Research Infrastructure Network and the European research infrastructure for biobanking to the Department of Health (DOH); the Department is currently considering this proposal. There are currently no plans for Ireland to join E-rare. The likely benefits and opportunity cost of such partnerships needs careful consideration in terms of the ability of Ireland to compete for European funding grants. The current position on the creation of a network on genetics and genomic medicine is that: ▪ The establishment of a NGGMN would bring together all parties within the field of genomic medicine ▪ NGGMN should operate on hub and spoke basis with dedicated outreach clinics ▪ The creation of a National Genetic and Genomic Medicine Network would provide a modern integrated genetic medicine service, engaged in patient care, education and translational research. ***Recommendation 11*** The HRB is increasingly integrating PPI (Public and Patient Involvement) in its work and this is reflected in the new strategy. The MRCG and the Irish Platform for Patient Organisations, Science and Industry (IPPOSI) are leaders in demonstrating the value of PPI. It will benefit from wider acceptance, particularly at the level of the health research funding agencies and within policy groups relating to health research. ***Recommendation 12*** (A full summary of the participation of Irish Centres of Expertise in proposed European reference networks (ERNs) and the support provided to them is available under recommendation 21.) The Clinical Lead and NRDO have supported the active development of National Centres of Expertise (CoEs) to participate in ERNs. European reference networks for rare diseases will serve as research and knowledge centres, updating and contributing to the latest evidence. The EU has stipulated criteria that all ERN members must meet with regard to, among others, research and training capacity, information systems and e-health tools. The establishment of ERNs should thus facilitate Irish clinicians to undertake research and recognition of the value of undertaking research, in terms of career progression, are essential to improve the scale of rare disease research currently being undertaken.

	Recommendation 13 The HRB submitted a business case to join European Clinical Research Infrastructure Network (ECRIN) to the Department of Health; the Department is currently considering this proposal. ***Recommendation 14*** Both the Rare Disease Taskforce and IPPOSI facilitate collaboration between rare disease patient groups and industry which is useful in this regard. National initiatives (primarily led by Science Foundation Ireland) have also sought to increase the engagement between academia and industry. Irish involvement in International Rare Diseases Research Consortium may be considered as a way to facilitate more industry collaboration. ***Recommendation 15*** The development of a co-ordinated structure relating to biobanking is a prerequisite to Irish membership of the European research infrastructure for biobanking. The HRB continues to represent Ireland in the context of development of international standards for biobanking. ***Recommendation 16*** **a.** Genetic counselling and pre-conceptual advice for families with rare diseases are available at the Centre for Medical Genetics at Our Lady's Hospital for Sick Children, Crumlin. Due to increasing demand as a result of additional referrals to the service, among other things, waiting times for these services have increased. The case for funding of additional professional staff at the centre has been submitted to the HSE. **b.** Ireland's first National Maternity Strategy – Creating a Better Future Together – which is a roadmap for the improvement of services over the next ten years, was launched by the then Minister for Health in January 2016. The strategy sets out a vision of maternity services that is about safety, quality and choice, and that places women very firmly at the centre of the service. The strategy describes a range of actions to be taken including that a dietetic service be available in each maternity network, so that the needs of women with type 1, type 2 and gestational diabetes, as well as those with other nutritional issues be addressed. Another action is that each maternity network scopes the necessity for the development of enhanced services at network level including dietetics, perinatal psychiatry, psychology, perinatal pathology, endocrinology, drugs liaison, physiotherapy and medical social work. The strategy also lists an action that any review of the maternity and infant care scheme considers the feasibility of extending coverage to include a preconception consultation and postnatal check at three to four months and/or additional postnatal GP visits where further pregnancy-related needs have been identified. These actions are directly applicable to this recommendation. **c.** The DOH has established a Working Group on Folic Acid (FA) chaired by Prof Michael Turner. Its Terms of Reference are: 1. To develop a FA Policy which will include the following elements: ▪ Development of population guidelines for peri-conceptual FA in pregnancy including at risk groups ▪ Make recommendations for appropriate information campaigns for the general public and healthcare professionals ▪ Consider the requirements for food fortification with FA. ▪ Consider the requirements for surveillance of neural tube defects and dietary FA intakes ▪ Consider research requirements ▪ To take account of EU, World Health Organization and other relevant international developments 2. The Group will be inclusive of FSAI, Safefood, HSE, Irish College of General Practitioners (ICGP), Institute of Obstetricians and Gynaecologists and representatives of Department of Health.

	3. In conducting its work the Group will take account of the ongoing developments as outlined above, consider short, medium and long term measures and prioritise actions to ensure adequate folate intakes in at risk groups. 4. The Group may seek expert advice on issues as deemed necessary. 5. The Group will submit its' recommendations to the Minister for Health for his consideration and approval. ***Recommendation 17*** The Department of Health is considering a policy framework for population-based screening programmes. ***Recommendation 18*** The Department is currently undertaking a review of the policy in relation to the National Screening Committee Archive. Furthermore, the Department held a forum with key stakeholders to engage in deliberative dialogue in relation to the retention, storage and use of Newborn Screening Cards for research purposes. The outcomes from this will inform policy options. ***Recommendation 19*** The European Commission Expert Group on Rare Diseases adopted recommendations on Cross Border Genetic Testing of Rare Diseases in the EU. This covers, among others, the themes of access to appropriate testing and expert clinical genetic counselling; sharing of expertise; improving/ensuring the quality of laboratories conducting genetic testing. The recommendation recognised that cross border genetic testing (CBGT) for RD will remain necessary in the foreseeable future, due to differences in the national/regional testing offer. On this basis, specific recommendations were written for the European Commission and the Member States in their reflections or policy developments on how to ensure timely and accurate genetic diagnostics for Rare Diseases. One recommendation provided that whether genetic testing is provided on the national/regional level or on a cross-border basis, expertise should be shared at the EU (or global) level; and that the organization of the collaboration between expert laboratories should be set within the context of European Reference Networks (ERNs), as per Directive 2011/24/EU by integrating expert laboratories in the different thematic networks linked to their area of expertise. The potential for ERNs to support the process of CBGT for Rare Diseases should be explored. (This further refers to Recommendation 23 below.) ***Recommendation 20*** A Rare Disease National Office was launched in June 2015. Annual ongoing funding of €200k is being provided and once-off funding for minor capital costs have been provided. The overall Model of Care for rare diseases is in development by the National Clinical Programme for Rare Diseases. The Model of Care for Transition has been completed and currently is in the public consultation stage. According to the proposed model of care, disease-specific clinical pathways published in peer-reviewed journals by Irish specialists, or international/European clinical pathways which have been reviewed by Irish rare disease specialists are linked in the public domain on the Orphanet Ireland webpage. The National Clinical Programme for Rare Diseases (NCPRD) has developed a Transition Model of Care document which is currently in review. A part time (2 year) temporary nurse has commenced at the NRDO to develop this rare disease transition model of care. ***Recommendation 21*** The National Clinical Programme for Rare Diseases has supported the HSE in the development of a process for the designation of CoEs in rare diseases; these would then be considered for membership of European Reference Networks. The process for designation of CoEs

	developed by the HSE includes a self-assessment by specialised services/centres/specialist networks based on a number of EUCERD criteria. These include: ▪ Capacity to provide management of rare diseases ▪ Evidence of expertise including relevant publications and international recognition ▪ Availability of multi-disciplinary care including health and social care services ▪ Capacity to produce and adhere to good practice guidelines for diagnosis and care ▪ Evidence of the development, measurement and improvement initiatives in quality of care, including patient satisfaction and quality control ▪ Evidence of teaching and training activities ▪ Evidence of involvement in research and clinical trials if appropriate ▪ Capacity to provide expert advice remotely/e-Health solutions ▪ Development of transition pathways as patients from paediatric to adults services ▪ Out-reach/shared care services ▪ Links and collaborations with patient organisations ▪ Arrangements for cross border care and referrals. <u>Call for Interest</u> In August 2015, the Acute Hospital Division of the HSE made a call for interest for applications for self-assessment to rare disease healthcare providers nationally. The completed self-assessment templates were reviewed by experts and successful centres or networks were invited to submit applications for national designation as CoEs. The applications were reviewed by the NCPRD Clinical Advisory Group and Acute Hospitals Division. At the time, seven candidate centres were identified and submitted to the HSE Acute Hospitals Division for review. The National Clinical Programme for Rare Diseases and the Department of Health encouraged designated centres of expertise to participate in ERNs for Rare Diseases in line with the national plan. Any centres applying for membership of an ERN must have strategies in place to ensure that care is patient-centred; that patients' rights and preferences are respected; and must show a research component to their work. Hence, the recommendations in the national plan that related to empowering and protecting patients and carers, and research on rare diseases will be fulfilled in part through this process. It is expected that ERNs will have a major structuring effect by linking thematic expert centres across the EU. With the encouragement of the HSE National Clinical Programme and the Department of Health, five centres of expertise were designated in June 2016 during the first round of calls from the European Commission for participation in European Reference Networks; three of these designated centres applied for membership of ERNs and two were approved. This process has also involved Orphanet. This is an EU sponsored encyclopaedic resource on rare diseases which also has a process to register CoEs. Professor Eileen Treacy is Ireland's national coordinator for Orphanet. In addition, rare diseases have already been tabled on the agenda for North-South meetings. Future work to deepen cooperation between both jurisdictions is anticipated. ***Recommendation 22*** Formal bidding for funding that is structured within a rare disease framework has already featured in the annual round of the Estimates process that commenced in 2015. The result is that the HSE National Service Plan 2016 provided to 1) continue to develop the National Rare Diseases Office that will act as a national point of reference for enquiries relating to services, diagnostics and clinical trials and linked to recognised online information databases. The office will be supported to assist with potential Centres of Expertise to join ERNs as 2)

	continue to develop the adult metabolic service in the Mater Misericordiae University Hospital for the transition of adolescents from paediatric services. The information provided at recommendation (10) on funding for rare disease research project is also applicable. In November 2014, the Minister for Health announced €850,000 for investment into charity-led research priorities, which particularly benefits rare disease research. Five charities were to provide matching funding bringing total investment to €1.9M. They were to share €850,000 in State funding to take part in international research into rare medical conditions, including respiratory infections and retinal blindness. It is a practical example of collaboration between the State and the charity sector with the intention of benefiting Irish people affected by rare disease. The five charities taking part are Alpha One, Cystinosis Ireland, Fighting Blindness, the Irish Thoracic Society, and the Royal Victoria Eye and Ear Hospital Research Foundation. Only rare diseases that have patient organisations, who are members of the MRCG (and who can afford to fund research) have the potential to access this funding. This funding scheme is not just for rare diseases but for all disease areas represented by MRCG charities. In 2016, the next cohort of projects was funded by the State with €1.686M, matched by charity funding of €1.224M. The total funding of €2.91M is shared between 11 charities, including Cystinosis Ireland, Fighting Blindness, Muscular Dystrophy Ireland, Irish Nephrology Society and others. Six of the 15 projects with a total value of €1.1M address rare diseases. The next round of this joint funding initiative will open in autumn 2017. ***Recommendation 23*** *See Recommendation 21 progress to date (duplicated).* ***Recommendation 24*** Respite care for children and adults with disabilities is provided by the HSE directly in some instances, or by agencies funded by the HSE to provide services on its behalf. In many instances respite services are part of the overall suite of services provided by voluntary service providers to people with disabilities under their service level agreements with the HSE. The HSE remains committed to working with all voluntary disability service providers to ensure that all of the resources available for specialist disability services, including respite services, are used in the most efficient and effective manner possible. The HSE's Social Care Operational Plan for 2017 aims to provide 182,000 overnight stays in centre-based respite services, in addition to 41,000 day respite sessions. ***Recommendation 25*** **a.** The HSE's Eligibility Criteria guidance document helps ensure that each individual has access to palliative care based on need. Access is not condition / disease specific and therefore people with rare diseases are triaged and prioritised based on need. **b.** Two NCCE guidelines for adult palliative care services have so far been developed by the adult National Clinical Palliative Care Programme: one on cancer pain, and one on constipation, and a third guideline is planned for end of life care. There are no plans to develop specific guidelines for rare life-limiting conditions. In practical terms, where a patient has a rare life-limiting condition with clinical manifestations that palliative care teams have not encountered before, they would be guided by the patient's consultant / paediatrician and/or GP. Palliative care services also work in close co-operation with families and carers. **c.** The National Development Committee for Children's Palliative Care takes forward the recommendations of the 2009 children's palliative care policy. While the policy itself recognises the four different ACT categories of children with life limiting conditions, the recommendations do not distinguish between conditions and have been implemented for all children with life limiting conditions, whether their diseases are rare diseases or not. **d.** The management and treatment of Rare and Less Common Cancers will be considered in the development of the next Cancer Strategy. The focus is on the potential for further centralisation of the management and treatment of rare cancers given the need to ensure that

patients are seen by clinicians with sufficient experience and expertise in these cancers. Some work has already been undertaken by the National Cancer Control Programme in recent years in this area.

Recommendation 26

Letters to the various colleges responsible for training in this area have issued. The bodies concerned are ICGP, Royal College of Surgeons in Ireland and Royal College of Physicians in Ireland (RCPI). The letter from the Dept. of Health requested the bodies/colleges to consider this recommendation in the context of the organisation of training for health professionals.
The Royal College of Surgeons (RCSI) Ireland reported that its medical school creates awareness for the student of the several thousand different diseases leading to ill-health. It referred to students being equipped with all the competencies to recognise and establish a diagnosis for rare disease processes – though it advised that due to the rare nature of these conditions, clinical exposure can be low. The RCPI reported to the Department that it facilitates training on rare diseases via a number of specialty study days for doctors on its Higher Specialist Training Programmes. It added that while it is difficult to comprehensively cover all rare diseases in its curriculum, the College ensures that doctors on its training programmes know how to assess the relevant information and resources available for the area.

Recommendation 27

See Recommendation 26, paragraph 1 above.
The RCSI reported that within each postgraduate discipline the management of rare conditions would be mastered by individuals within their subspecialty. Meanwhile, the RCPI replied that it had included a session on rare diseases in its 2016 Masterclass Series. The session, entitled *Clinical Update: Rare Diseases* was to take place in April 2016 delivered by the NCPRD. The college also referred to the difficulty to comprehensively cover all rare diseases in the curriculum; but that it ensures that doctors on its training programme know how to access the relevant information and resources available.
The NRDO has developed a general practitioner/allied health professional module for Rare Diseases to be made available on the NRDO website in the near future.

Recommendation 28

The National Clinical Programme for Rare Disease was established in 2014. The National Clinical Programme for Rare Diseases builds upon the work done through the public consultation processes in recent years. A multi-disciplinary working group delivers the work of the programme and is made up of range of healthcare professionals working in the area of patient care and rare diseases. The work of the programme is overseen by a Clinical Advisory Group, a committee of the Royal College of Physicians of Ireland, made up of consultant specialists from a broad range of disease specialities and both paediatric and adult services. The programme's objectives are as follows:

- Access: Patients with rare diseases and their families should have access to quality information and support, to enable accurate and timely diagnosis and access to appropriate specialist care.
- Quality: Clinical expertise for rare diseases should be provided through a network of national Centres of Excellence/Health Care Providers or at designated centres abroad.
- Value: Timely access to appropriate diagnosis and care should result in decreased mortality, morbidity and disability and be cost-effective. The scope of the National Clinical Programme for Rare Diseases includes the following disease categories:
  - Single gene disorders
  - Chromosomal disorders
  - Hereditary metabolic disorders
  - Haemophilia and hereditary coagulation disorders

	○ Rare congenital disorders ○ Rare endocrine disorders ○ Neurological disorders and neuro-metabolic disorders ○ Rare skin disorders ○ Rare kidney diseases ○ Rare eye disease ○ Rare connective tissue/skeletal/autoimmune disorders ○ Rare lung disorders including alpha-1-antitrypsin disorder and excluding Cystic Fibrosis. ***Recommendation 29*** A Rare Disease National Office was launched in June 2015. Annual ongoing funding of €200k is being provided and once-off funding for minor capital costs have been provided. The functions of the office include: ▪ Centralisation of up-to-date Irish rare disease information through Orphanet Ireland (www.orpha.net) ▪ The establishment of a rare disease information help line to provide patients, families and healthcare providers with information and support relating to rare diseases ▪ A website with information and links to relevant rare disease services and organisations around Ireland and Europe ▪ Development of national rare disease care pathways and in time, the development of rare disease registries. The National Rare Diseases Office was launched by Minister Varadkar on June 4th 2015. It will be housed within the Mater Misericordiae Hospital until a location is available at the National Paediatric Hospital. ▪ The NRDO provides information for patients, families and health professionals as outlined above. Information on Irish rare disease resources including: Centres of Expertise, Patient Organizations, Clinical Trials, Research Projects, Registries and Biobanks and Diagnostic Laboratories is available on Orphanet. ▪ An information phone line and rare diseases email contact was opened in September 2015 and an 1800 number in February 2016. ▪ The NRDO website launched in December 2015, is hosted on the HSE website. It contains information for patients and their families as well as for healthcare professionals. It has a dedicated page describing the Irish process for ERN enrolment. ▪ The National Rare Diseases Information Line is currently developing services under the best practice guidelines of the European Rare Diseases Helpline Forum ▪ The National Rare Diseases Information Line serves as a reference for the Irish Cross-Border Directive and Treatment Abroad Scheme teams ▪ The National Rare Diseases Office also provides education and awareness of rare disease through dissemination activities (update as of May 2016, below) ○ 23 Departmental presentations ○ 5 Patient organisation presentations ○ 1 Hospital grand rounds ○ 3 Presentations at scientific meetings ○ 4 Posters at scientific meetings ○ 10 Leaflet tables/information booths ○ 4 University rare disease lectures ○ 1 Medical publication ○ 3 Newspaper and other media publications

	○ 1 National Health Services-hosted webpage ○ 1 Rare Disease office launch with Minister of Health ○ 1 College of Physicians half day Masterclass. ***Recommendations 30-38*** The HSE Acute Hospitals Division is developing the terms of reference, required membership and reporting relationship for this committee. This Committee will also be supported by the NCPRD Clinical Advisory Group. The terms of reference for the proposed Rare Diseases Technology Review Group are at final draft stage. The question of elaborating the Terms of Reference further in order to reflect some of the recommendations in the National Plan in this area has been discussed. A chairperson has been provisionally identified subject to provision of expert pharmacologic support to advise the candidate. The rare disease drugs to be considered by the Rare Diseases Technology Review Group have not been determined yet. The membership of the group will include: ▪ A minimum of three members who are consultants in rare or highly specialised diseases, recommended by the relevant professional society, faculty or college, who have content experience in the specific discipline and are approved by the Clinical Lead for the National Clinical Programme for Rare Diseases. In addition the Clinical Lead for the National Clinical Programme for Rare Diseases will be a member; ▪ Chief Pharmacist and an additional Pharmacist, a minimum of one member with Health Economical, Pharmacoeconomics or statistics and epidemiology expertise; ▪ A minimum of one invited participant from a related designated centre of expertise, recommended by the Clinical Advisory Group for the National Clinical Programme for Rare Diseases, as required, according to the speciality area; ▪ One representative appointed by HIQA; ▪ Patient Group representatives; ▪ Primary Care Reimbursement Services representative; ▪ Up to three additional members may be appointed. The group will report to the HSE Committee for Optimising Pharmaceutical Value. Patient interest groups recently met with the National Director for Acute Hospitals and were asked for their comments on the final draft document. The National Rare Disease Office has done some work on establishing a database of Orphan Drugs (excluding cancer and Cystic Fibrosis) that are reimbursed; the purpose of this work is to record such information on the Irish Rare Diseases Office Orphanet site. The recommendation relating to limiting the authority to prescribe to a specialised physician applies in the case of adult and children's metabolic centres. ***Recommendation 39*** Progress has been made in recent years to advance the capability and quality in Ireland in relation to the design, conduct, analysis and reporting of clinical trials. The state (via agencies such as the HRB, HPRA) as well as patients, researchers, industry and clinician representatives have worked together for this. Ireland has the potential to do much more with respect to participation in European trials. ***Recommendation 40*** This recommendation is partly encompassed by firstly the recommendation on ERNs by the Commission Expert Group on Rare Diseases in relation to ERNs and the operational criteria for the assessment of Networks and Health Care Providers (HCP) to be used by the EU Board of Member States. The latter provides that each HCP which applies for membership of an ERN must have strategies in place to ensure that care is patient-centred and that patients' rights and preferences are respected; provides patients with clear and transparent information

	about the complaints procedures and remedies and forms of redress available for both domestic and foreign patients; regularly collects information on patient care experience within the Network's area of expertise and uses this information to make ongoing improvements; maintains transparency, including providing information to patients and the general public about clinical outcomes, treatment options, and quality and safety standards that are in place. ***Recommendation 41*** NGOs and patient representatives in the area of rare diseases participated in the National Review Group that wrote the first National Rare Disease Plan for Ireland. A National Oversight Group was established in 2015; it was charged with monitoring the implementation of Ireland's National Rare Disease Plan. The group is comprised of, among others, representatives from the rare disease NGO community and patients' representatives. The HSE's National Clinical Programme for Rare Diseases also has patient representatives on its National Working Group for Rare Diseases. The working group is charged with carrying out the work of the programme under the auspices of the HSE. ***Recommendation 42*** *See Recommendation 23.* ***Recommendation 43*** *See Recommendation 29.* ***Recommendation 44*** All of the recommendations in the National Plan were written in the context of making awareness, research and services better for people with rare diseases. Progress with a number of recommendations points to advances that go beyond the healthcare setting for people with rare diseases. It is emphasised that services be person-centred. For example the National Rare Diseases Office was set up to provide support and information to people with rare diseases. Its functions includes the establishment of a rare disease information help line to provide patients, families and healthcare providers with information and support relating to rare diseases. It is also pertinent that the National Clinical Programme for Rare Diseases and the Department of Health encouraged designated centres of expertise to participate in ERNs for Rare Diseases in line with the national plan. Any centres applying for membership of an ERN must have strategies in place to ensure that care is patient-centred and that patients' rights and preferences are respected. In effect, these centres must embrace a person-centred ethos as part of the qualifying criteria to join ERNs. ***Recommendation 45*** Funding for rare diseases has formed part of the annual Estimates process that determined health allocations for expenditure in 2016. Similarly, the HSE has committed in its 2017 National Service Plan to support the designated Centres of Expertise, especially in the context of their involvement with European Networks for Rare Diseases. In addition, as referred to earlier, the National Rare Disease Office has been established for the purposes of among others, providing information on and promoting awareness of rare diseases. ***Recommendation 46*** A Rare Disease National Office was launched in June 2015. Annual ongoing funding of €200k will be provided and once-off funding for minor capital costs have been provided. One of its functions will be to act as an information source on and raise awareness of rare diseases. In addition, Orphanet, which is funded by the EU Commission, provides comprehensive information on rare diseases that is directed at patients, clinicians and others in the rare disease community.

	Recommendation 47 The Programme for Government, *A Programme for Partnership Government* provides at paragraph 5.3.26 to implement the National Rare Diseases Plan. An Oversight Group to monitor the implementation of the National Rare Disease Plan was established in 2015. The group is largely comprised of members from the original steering group that led the drafting of the national plan. There have been a number of meetings of the group with a full agenda for each meeting, for which a progress report on the implementation of each recommendation in the national plan featured prominently. *(See 'Governance and organisational structures' for list of Oversight Group members)* ***Recommendation 48*** This interim report represents a detailed review of the implementation of the national plan. It is partly based on the interim progress reports provided to the National Oversight Group on the implementation of Ireland's National Rare Disease Plan.
Governance and organisational structures	The Rare Diseases Steering Group was established by the Minister in 2011. Its purpose was to develop a policy framework for the prevention, detection and treatment of rare diseases based on the principles of high quality care, equity and to be patient centred. The policy is being operated over a 5 year period. The Steering Group was composed of stakeholders from diverse patient organisations, State agencies (Irish Medicines Board, Health Research Board), the Health Service Executive and the Department of Health. An Oversight Group to monitor the implementation of the National Rare Disease Plan was established in 2015. The group is largely comprised of members from the original steering group that led the drafting of the national plan. There have been a number of meetings of the group with a full agenda for each meeting, for which a progress report on the implementation of each recommendation in the national plan featured prominently. The members of the Oversight Group are as follows: Dr. John Devlin (Chair), Department of Health Prof. Eileen Treacy, Health Service Executive Dr. Anne Cody, Health Research Board Mr. Tony Heffernan, Patient Representative (Bee for Battens) Mr. John McCormack, Medical Research Charities Group Ms. Avril Daly, Genetics Rare Disorders Organisation (GRDO) Dr. Geraldine O'Dea, The Health Products Regulatory Authority Mr. Derick Mitchell, Irish Platform for Patients' Organisations Dr. Helen McAvoy, Institute of Public Health in Ireland Ms. Helen Byrne, Health Service Executive Mr. Philip Watt, Cystic Fibrosis Ireland Mr. Liam McCormack, Department of Health Ms. Caitriona Connolly, Department of Health
Funding model	*See Recommendations 4, 6, 8, 10, 16a, 20, 22, 29 and 45.*
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***

Screening programmes (including newborn screening)	*See Recommendations 17 and 18.*
Personalised medicine, genomics, genetic counselling	*See Recommendations 6, 10, 16 and 19.*
Models of care/care pathways	*See Recommendations 20, 21, 22, 23, 24, 25, 28, 29, 42, 43, 44, and 45.*
Workforce	*See Recommendations 12, 26 and 27.*
European Reference Networks	*See Recommendations 12, 19, 21, 22, 23, 40 and 42.*
EU alignment and participation	*See Recommendations 6, 7, 11, 13, 19, 21, 30, 42, and 47.*
Health information (including rare disease registries)	*See Recommendations 1, 2, 3, 4, 5, 6, 7, 8, and 9.*
Orphan medicines	*See Recommendations 30-39.*
Rare disease research	*See Recommendations 10, 11, 12, 13, 14, 15 and 22.*
Alignment beyond the healthcare sector	*Not mentioned in progress updates. Originally addressed in Recommendations 40, 41, 44, 45, and 46.*
Any additional information (for example, background to the strategy or strategy development)	*N/A.*

Key: CBGT: cross border genetic testing; CoE: National Centres of Expertise; DG SANTE: Directorate-General for Health and Food Safety; DOH: Department of Health; ECRIN-ERIC: European Clinical Research Infrastructure Network; ERN: European Reference Networks; EU: European Union; EUCERD: European Union Committee of Experts on Rare Diseases; FA: Folic Acid; HCP: Health Care Providers; HRB: Health Research Board; HSE: Health Service Executive; ICGP: Irish College of General Practitioners; IPPOSI: Irish Platform for Patient Organisations, Science and Industry; JRC: Joint Research Centre; MRCG: Medical Research Charities Group; NCPRD: National Clinical Programme for Rare Diseases; NGGMN: National Genetic & Genomic Medicine Network; NRDO: National Rare Disease Office; PPI: Public and Patient Involvement; RCPI: Royal College of Physicians in Ireland; RCSI: Royal College of Surgeons.

Table B17. Data extracted for the Netherlands (National Plan for Rare Diseases)

The Netherlands	Strategy information
Author(s) **Title**	ZonMw (the Netherlands) National plan for rare diseases[52]
Timeline	Published in 2013.
Overall aim(s)	To make recommendations for activities that can improve the position of people with a rare disease in the broad field of diagnostics, treatment, care, research and information provision. The strategy aims to designate various field parties as primarily responsible for such activities.
Themes and or priorities	**Abbreviations for use throughout the entire strategy.** **Add-on:** An Add-on is linked to a DBC care product and is intended for a number of special forms of care, such as expensive medicines (>€10,000 per patient per year) (state of affairs August 2013) **AJN:** Doctors Youth Health Care Netherlands. Scientific association of doctors working in JGZ. **Biofarmind:** Association of Biotechnological Pharmaceutical Industry (www.biofarmind.nl) **CAVOMP:** Project on the added value of orphan drugs (measured in the daily practice) (CAVOMP=Clinical Added Value of Orphan Medicinal Products). **MEB:** Medicines Evaluation Board (www.cbg-meb.nl) **CCMO:** Central Committee on Human Research (www.ccmo-online.nl) **CG Council:** Chronically Ill and Disabled Council (www.cg-raad.nl) **CHMP:** Committee of the European Assessment Authority that assesses market authorisation **CINEAS:** Coding system from Clinical Genetics Netherlands **COMP:** Committee of the European Assessment Authority for the designation of an orphan medicinal product (see EMA website) **CVZ:** Health Insurance Board (package management) (www.cvz.nl) **DBC and DBC Maintenance:** Diagnosis Treatment Combination The DBC Maintenance Foundation offers insight into DBC care products and other forms of care services (www.dbcmaintenance.nl) **DG Research and Innovation:** Directorate-General for Research and Innovation of the European Commission develops, among other things, a research program in the field of research and innovation (including business) http://ec.europa.eu/research/index.cfm **DG SANCO:** Directorate-General for Health and Consumers of the European Commission develops research programs in the field of public health, among other things. http://ec.europa.eu/dgs/health_consumer/index_en.htm **EMA:** European Medicines Evaluation Authority, based in London. Reports of COMP and CHMP meetings and patient information on registered orphan medicinal products can be found on the EMA website (www.ema.europa.eu) **E-Rare:** European cooperation in the field of rare disease research **Erfocentrum:** www.eerderheid.nl **EUCERD:** European Committee for Experts on Rare diseases. (www.eucerd.eu) **EUROCAT:** Registration of congenital disorders in the Northern Netherlands **EUROPLAN:** European project on National Plans for rare diseases (www.europlanproject.eu) **EURORDIS:** European umbrella organisation for patients (organisations) of rare diseases **FBG:** Forum Biotechnology and Genetics

	PGO: Fund Subsidy for patient organisations (http://www.fondspgo.nl/) **ICD code:** International Classification of Disease (WHO) **ICF code:** International Classification of Functioning (WHO) **LHV:** National Association of General Practitioners (http://lhv.artsennet.nl/home.htm) **LPGGz:** National Mental Healthcare Platform (http://www.platformggz.nl/lpggz/) **NCJ:** Dutch Centre for Youth Health (www.ncj.nl/) **NEFARMA:** Association of innovative medicines in the Netherlands (www.nefarma.nl) **NFU:** Dutch Federation of University Medical Centres (UMCs) (www.nfu.nl) **NHG:** Dutch Society of General Practitioners (www.nhg.org) **NPCF:** Dutch Patients and Consumers Federation (www.npcf.nl) **NZa:** Dutch Healthcare Authority (www.nza.nl) **NVZ:** Dutch Association of Hospitals (www.nvz-ziekenhuizen.nl) **Orphacode:** Code for rare diseases in Orphanet (www.orpha.net) **Orphanet (EU and NL):** www.orpha.net **PGO:** Platform for people with intellectual disabilities, their parents and representatives (www.platformvg.nl) **RIVM:** National Institute for Public Health and the Environment (www.rivm.nl) **SGF:** Collaborating Health Funds **STZ:** Top Clinical Hospitals Foundation (www.stz-ziekenhuizen.nl) **UMC:** University Medical Centre. The eight UMCs have united in the umbrella organisation **NFU:** Dutch Federation of University Medical Centres (www.nfu.nl) **VKGN:** Dutch Association of Clinical Genetics (www.vkgn.org) **VKS:** Adults and children with metabolic diseases (www.metabolic diseases.nl) **VSN:** Association for Muscular Diseases in the Netherlands (www.spierverzekeringen.nl) **VWS:** Ministry of Health, Welfare and Sport **VSOP:** Association of Collaborating Parent and Patient Organisations for rare and genetic disorders (www.vsop.nl) **Wbmv:** Special Medical Procedures Act **WHO:** The World Health Organisation www.euro.who.int **ZonMw:** ZonMw finances health research and encourages the use of the knowledge developed to improve care and health **ZN:** Umbrella organisation of health insurers (Zorgverzekeraars Nederland) (www.zn.nl) **ZZF:** Rare Diseases Fund (www.zzf.nl) **Theme 1: Unfamiliarity with rare diseases** *Description:* The problems that people with a rare disease encounter can partly be explained by healthcare providers' unfamiliarity with a large number of rare diseases; It is precisely this rarity that results in unfamiliarity, late diagnosis and – even after a correct diagnosis has been made – little practical experience in caring for and treating patients with the disease. In foreign (English) documents, unfamiliarity with rare diseases is often described as a lack of awareness. This term is also increasingly used in the Netherlands, but the word alertness to the possibility of a rare disease in a specific patient expresses this problem more precisely. Lack of awareness or alertness has to do with the lack of knowledge, experience and the sense of urgency to conduct further research or refer the patient. This ultimately has adverse effects with regard to timely diagnosis, care and treatment.

	What is already there: The Orphan Drugs Steering Group (2001-2011) has paid attention to making the concepts of rare disease and orphan drugs better known to the general public, to relevant parties in the field and to politicians and government. Although attention for patients with rare diseases has increased, efforts are still needed to keep rare diseases permanently on the agenda. Since 2008, Rare Disease Day has been organised annually. This event contributes to raising awareness of the concept of rare disease. Family, patients and parents have successfully contributed to improving awareness of rare diseases through the media. In addition, these people directly involved contribute to raising awareness of the disease through promotion among professional groups, for example by drawing up brochures about the condition. They also collect information from their supporters about the symptoms of the disease for diagnostic purposes. The latter is happening more and more often and increasingly systematically. *What is missing:* Many rare diseases manifest themselves in 'vague' and difficult to classify complaints and symptoms. Due to the great diversity of rare diseases, it is unrealistic to expect that doctors can directly trace these symptoms to a specific diagnosis. Although the majority of rare diseases are genetically determined, the increased possibilities for genetic diagnosis are not yet sufficiently applied in practice. A large number of rare diseases have not yet been scientifically investigated, or have only been studied to a limited extent, as a result of which many aspects relating to these diseases are still unknown or little known. In many cases, the impact of having a rare disease on daily life has not been studied. Attention to rare disorders must therefore be greatly improved in the domains of public healthcare, healthcare policy (government), work, school and housing. Especially now that a number of elements of care are being transferred from the AWBZ to municipalities (WMO). **Theme 2: Information provision and communication** *Description:* Due to the unfamiliarity of rare diseases, patients and parents, but also healthcare professionals, encounter problems. This relates to various aspects such as: unfamiliarity with the symptomatology, aetiology, pathophysiology, genetics, the variable course of many rare diseases and unfamiliarity with treatment. There is a need for accessible information and for improving knowledge in various areas; including through education, training, knowledge transfer and the use of e-learning and eHealth. Help finding the right information can be valuable. Various groups can be distinguished that are looking for information. People with symptoms or parents who are looking for an explanation of complaints and a diagnosis of perhaps a rare disease. In addition, there are people who have a diagnosis, but are looking for additional information or fellow sufferers. People with very rare diseases, for which there is often no patient organisation, more often encounter problems and often need help in searching for information. Another group looking for information are healthcare professionals, researchers and pharmaceutical companies. They are looking for information about the disease in general, treatment options, expertise centres or requirements or financial resources for (drug) research. *What is already there:* The internet has made information about rare diseases more easily available to a wide audience. New social media and new digital ICT techniques are increasingly being developed to bundle knowledge about rare diseases or create networks in the field of rare diseases. Particularly for diseases that are rare in each country, the 'world wide web' is an important instrument for finding each other and exchanging information. Patient organisations have often collected a wealth of information and work together with doctors to improve information about care and treatment of rare diseases. The GP brochures on rare diseases and the development of care standards for rare diseases are examples of this. In the Netherlands there are various websites where information can be found about various rare diseases and associated organisations, such as the public information centre Erfocentrum. The Erfocentrum also has a counter function for questions, by e-mail and telephone. The website provides information about hereditary disorders and genetic research. In addition, the more scientifically oriented Orphanet provides information about rare diseases also in the Dutch language. There are various websites that provide information about medicines for rare diseases (orphan medicines). Such as the European Medicines Agency (EMA), the Medicines

	Evaluation Board (CBG) and the professional organisation of pharmacists (KNMP). The orphan medicine information point portal has been online since October 2013. This website provides information intended for researchers and companies about the development, regulation, financing and reimbursement of orphan drugs. Information from the website of the former steering group on orphan drug. The internet has made information about rare diseases more easily available to a wide audience. New social media and new digital ICT techniques are increasingly being developed to bundle knowledge about rare diseases or create networks in the field of rare diseases. Particularly for diseases that are rare in each country, the 'world wide web' is an important instrument for finding each other and exchanging information. Due to the unfamiliarity of rare diseases, patients and parents, but also healthcare professionals, encounter problems. This relates to various aspects such as: unfamiliarity with the symptomatology, aetiology, pathophysiology, genetics, the variable course of many rare diseases and unfamiliarity with treatment. There is a need for accessible information and for improving knowledge in various areas; including through education, training, knowledge transfer (see also the previous chapter) and the use of e-learning and eHealth. Help finding the right information can be valuable. Various groups can be distinguished that are looking for information. People with symptoms or parents who are looking for an explanation of complaints and a diagnosis of perhaps a rare disease is transferred as much as possible to field parties, so that they can take over tasks in this area. Policy information about rare diseases and orphan drugs can be found on the government website. *What is missing:* As can be seen from the above, a lot of information is available. Not all information about rare diseases is of good quality or available in Dutch. Sometimes the information is not up to date or very limited. In addition, information is fragmented across different websites and their organisations. There is a need for a central location or connection of internet portals, from which people could be referred. The various initiatives should work more closely together. It is obvious that patient organisations, together with existing information centres and hospitals, can play a central role in this. It is also important that people can go somewhere to report problems within healthcare or, for example, to receive reimbursement for therapy. In this sense, a counter also has a signalling function. Such a position primarily belongs to patient organisations. In many cases, knowledge about a particular rare disease is limited to a single practitioner or a small group of practitioners and researchers in a hospital. An important bottleneck here is that it is currently not transparent where the expertise is located and what criteria it meets. In regional hospitals and youth healthcare or general practitioners, there is often a lack of general knowledge about and alertness to rare diseases. The exchange of information between experts and other healthcare providers - and thus the use of each other's expertise - is not yet taking place sufficiently. ICT (such as e-health and e-learning) can contribute to the exchange of knowledge. Applications are being developed for more and more groups of diseases, which could also be useful for exchanging knowledge about rare diseases. **Theme 3: Organisation of care and availability of therapy** *Description:* The number of rare diseases is large and although the diseases can be classified into groups the diversity of the disease within a group is often great. The natural history of rare diseases is variable and the treatment of the majority is only symptomatic. In the chronic phase, there is a lack of coordination and knowledge about symptomatic or palliative care or about new treatment methods and a multidisciplinary treatment team is lacking. Due to the genetic component of many rare diseases, clinical genetics is an important discipline, but often not yet represented in a multidisciplinary team. Care includes many aspects, from making the diagnosis to daily and specialist high-quality care, at home, in the hospital and in other healthcare institutions. Care also includes psychosocial and social care. In recent years, more attention has been paid to strengthening expertise within hospitals. The challenge for the coming years is to define centres and make the connection between these experts in hospitals and care close to home. Improving care for people with rare diseases also includes gathering and sharing new knowledge through research and training.

	What is already there: *Diagnostics:* The heel prick is available in the Netherlands for population screening of newborns. This allows 18 diseases (all rare) to be detected. A follow-up database has been developed (NEORAH) for two conditions included in the heel prick (AGS and sickle cell anaemia). The number of conditions to be detected in other EU Member States varies between one and thirty-six. The Health Council received a new request for advice from the Ministry of Health, Welfare and Sport in 2012 to advise on expanding the number of diseases that can be detected via the heel prick. Rare diseases are caused in 80% of patients by a hereditary change in a gene. Many genetic variants can be found with exome or genome sequencing. It is still difficult to identify variants that cause rare diseases. The possibilities for applying the screening of genetic material are increasing and it is expected that it can be used for more diseases and at lower costs in the future. Genetic testing is in principle included in the insured package. National screening takes place under the responsibility of the Dutch government (RIVM). The basic principle of government policy is that screening the population for diseases only has added value if health gains can be achieved through early detection. Screening for disorders is also a task of youth healthcare (known as child health clinics). In addition, there are a number of integrated early intervention teams (VTO Teams) spread throughout the country, which have expertise in the recognition, diagnosis and guidance of developmental delays. There are also options before and during pregnancy to diagnose abnormalities that could indicate rare diseases. In this context, the Biotechnology Forum (FBG) presented a report to the minister in 2013 on preconception genetic research. *Organisation of Care & expertise centres:* Concentration of care is becoming increasingly important in the organisation of healthcare. This concentration of care (knowledge and expertise) is necessary to improve quality. In the context of the legislation on cross border care, the EUCERD has established criteria for Centres of Expertise and for Networks of Centres of Expertise in Europe (www.eucerd.eu). A number of key concepts of criteria for expertise centres for rare diseases are: experience with care and treatment of children and adults with rare diseases, experience in research, multidisciplinary approach, being part of a network and collecting and sharing knowledge. A European project has been started under the coordination of the EUCERD to develop new ICD codes (ICD 11) for rare diseases. The Orphacode was developed from the Orphanet. This code can be used in addition to ICD43. The digital child file is available for keeping track of data about children in the Netherlands. This file records information about pregnancy, family history, birth, congenital abnormalities, growth and development as well as vaccination. A standard of care is being developed for more than 30 rare conditions (by the VSOP), which describes the necessary care and treatment by patients and practitioners44. Most rare diseases (80%) have a hereditary or genetic nature. There is a website available that provides information for general practitioners www.huisartsengenetica.nl. *Availability of treatment:* Since the introduction of European regulations on orphan drugs (in 2000), 70 new medicines for 55 different rare diseases have come onto the market. The reimbursement of medicines is regulated nationally. After France, the Netherlands has the most extensive availability of these European registered orphan drugs. Intramural via add-ons linked to Diagnosis Treatment Combinations (DBCs) (i.e. if the costs are higher than €10,000)46, extramural via the Medicines Reimbursement System (GVS). Since 2006, a number of expensive orphan drugs have been provided to patients through the budget of the university hospitals. The hospitals in question were reimbursed for the costs of these medicines (until 2013) through the orphan medicine policy rule. The condition for this was that data would be collected on therapeutic value, costs and effectiveness. Expensive orphan drugs that were included in the orphan drug policy rule until 2013 are evaluated by the Health Insurance Board (CVZ).Initiatives have been launched in Europe in which reimbursement authorities, researchers and pharmaceutical companies work together on the evaluation of orphan drugs in practice. An article on cross-border healthcare must be included in Dutch law by October 2013. This legislation must make treatment available across borders. The

	preparatory legislation also includes an article on expertise and reference centres. The NFU has started making an inventory of expertise and treatment centres for rare diseases in UMCs, which have the support of the Boards of Directors (June 2013). *What is missing:* Diagnostics: Timely diagnosis is one of the biggest problems for people with rare diseases. It appears not yet possible to give an exact diagnosis for a group of people with rare diseases. The experience of parents and patients is that people do not quickly think of a rare disease when they go to the clinic or their GP. This can contribute to the fact that it can sometimes take years before the diagnosis is made. The problem of unfamiliarity and lack of experience with rare diseases in practice plays a role in this. There is also a lack of transfer of knowledge (for example via ICT tools) and it is usually unknown where expertise in the diagnosis of specific disorders is available. Many rare diseases have a genetic component, which is often not yet known to healthcare providers and/or the patients and his/her family; or is not discussed. This can lead to a delay in making the diagnosis. New methods for genetic diagnosis are not yet being used sufficiently. Organisation of care: Making a diagnosis is one aspect, finding a place where one has knowledge about the care and treatment of a specific rare disease is another. Although care for patients with chronic diseases is widely available in the Netherlands, patients and parents involved with rare diseases experience a lack of coordination of care and fragmentation of scarce knowledge. On the one hand, this is due to insufficient cooperation between professionals. On the other hand, because of the way in which current healthcare is organised and financed. These 'partitions in healthcare' (for example between care and cure) do not promote an integrated approach, certainly not for diseases for which knowledge is scarce and an integrated approach is necessary. In addition, only a few hospitals are transitioning from care for children with rare diseases to adult care. In adult care, people are referred to different practitioners for different complaints that all belong to the same rare disease and there is often no multidisciplinary and integrated approach. This requires a lot of control from the patient. An expertise centre can play a crucial role in the coordination of care with a network of healthcare providers around the patient. In the longer term, centres can have added value in healthcare when it comes to timely diagnosis, prevention of complications, organisation of care (home – hospital), broadening knowledge about rare diseases and research into and application of a new treatment. Decentralisation brings parts of healthcare under the control of the municipality (WMO). These components must also be integrally included in a chain. However, chain care is not yet a practice. The lack of uniform coding of rare diseases and registration of people with rare diseases is a major bottleneck in healthcare. People diagnosed with rare diseases cannot currently be found/ recognised in existing hospital registrations (HIS) and general practitioner registrations (HIS, ICPC codes). In ICD10 there is a code for only 250 rare diseases. The lack of a specific code makes it difficult to find people with rare diseases in databases (hospital and other registrations) and does not promote cooperation within healthcare (chain care). In the Netherlands, there is no body that is formally authorised to designate (departments of) hospitals as expertise centres on the basis of uniform criteria. In theory, the Special Medical Procedures Act (Wbmv, article 8) offers possibilities for the government to designate centres for rare diseases within a legal framework. The Dutch Strategy regarding rare diseases of the Ministry of Health, Welfare and Sport (29.02.2012) states that the government's designation of one or more reference centres for the treatment of a specific rare disease or group of related diseases is not an option in the short term. *Availability of treatment – what is still missing:*

	Off label: Reimbursement problems regularly arise when it comes to the reimbursement of medicines that are not registered for rare diseases. Health insurers do not have to reimburse such a medicine and comply with CVZ's advice regarding the off-label use of medicines. Centres of expertise: In the current situation, care for a specific rare disease is not always purchased in an expertise centre. To solve this problem, a recommendation has been made to declare rare diseases as non-competitive and that health insurers can make joint agreements about purchasing care and treatment of rare diseases. It is already happening in some cases, but not yet for the group of rare diseases as a whole. Hospital boards of directors (and others institutions) where expertise centres are present can be held responsible for the continuity of the functioning of these expertise centres. Availability of orphan drugs (intramural): In the context of the orphan drug policy, a number of academic hospitals have conducted research into the effectiveness of several expensive orphan drugs. The final advice on orphan drugs for Pompe disease and Fabry disease has been drawn up by CVZ. Following the advice, the minister has decided to continue the reimbursement of the resources in 2013 via the basic package. Decision-making about the inclusion of expensive orphan drugs in the package based on outcome and cost-effectiveness research has limitations. The strategy of the Ministry of Health, Welfare and Sport describes that all orphan drugs will fall under hospital financing, but that this has no influence on the entitlement. This development could promote the establishment of centres of expertise, provided that centres provide treatment and care for people with rare diseases. It is argued that a consistent reimbursement policy should be developed that takes into account the specific situation of the treatment of rare diseases with (orphan) medicines. In drug treatment of rare diseases, it is relevant to regularly investigate whether the patient still benefits from the drug and whether the dose and frequency are optimal. A bottleneck here may be that the researcher is also the patient's practitioner. This can create a moral dilemma in the treatment relationship. **Theme 4: Scientific research in the field of rare diseases** *Description:* Research in the field of rare diseases is broad: medical-scientific or social-scientific research. The research can be basic (the search for hereditary aspects or other mechanisms of origin, for points of application for medicines) but also applied research with medicines (before registration and in everyday practice - post-registration) and research into the natural course. Research may also cover aspects related to living with a rare chronic disease and palliative care. Social scientific research can also relate to bottlenecks in healthcare. The results of this latter type of research can be relevant for policy development and advocacy. Ideally, these research disciplines come together in an expertise centre. *What is already there:* Subsidies for medical-scientific health research are mainly provided through ZonMw and disease-specific funds. There are funds that specifically focus on rare diseases, such as the Rare Diseases Fund, the Princess Beatrix Fund for muscular diseases, or the Dutch Cystic Fibrosis Foundation (NCFS). The NCFS is affiliated with the collaborating health funds (SGF). Dutch fundamental and early clinical research into rare diseases is well regarded abroad. Research into rare diseases is an area par excellence in which European and global cooperation and coordination are highly desirable. Patient numbers are often small in one Member State, both for drug research and for research into the natural history of a specific rare disease. European cooperation also takes place via ZonMw (E-Rare programme), but also via scientific institutions themselves. E-Rare finances projects in which various researchers from various European countries (Member States or Associated Countries) collaborate. In 2012, 11 projects were positively awarded, with Dutch researchers participating in eight projects. To reduce the 'gap' between fundamental research and therapy, a ZonMw program Priority Medicines Rare (PM-Rare) was launched in 2009. In May 2012, three promising projects were rewarded with a subsidy of € 3 million per project. The projects involve public-private

	partnerships. Many new diagnostics or treatment options are developed by (spin-offs from) universities or small companies. In recent years, 'large' pharmaceutical companies have also become interested in developing medicines for small groups. Current overviews of orphan drugs on the market are published via Orphanet and via the European Medicines Agency (EMA). For Dutch pharmaceutical SME companies, public or non-profit organisations, it is possible to apply for a small subsidy from ZonMw (subsidy scheme Orphan Designation, ODD support) for the costs incurred in preparing and submitting a file to the EMA for the application of an orphan designation, an orphan designation. The Dutch contribution to the development of orphan drugs has increased to twelve orphan designations in 2010. In the coming years, much can be expected from new technological developments that can contribute to faster diagnosis of rare diseases (such as array research, exome sequencing, proteomics, or expanding the heel prick) and from developments that contribute to a causal treatment for rare diseases, such as gene and cell therapy. Research into heredity and exogenous factors will also provide more insight into the cause of diseases, which will also make it possible to provide better information (heredity advice or preconception care) for the patient and his/her family. Establishing – maintaining – registers of rare diseases is of great importance for scientific research as indicated in the introduction to this chapter. Some examples are: the TI-Pharma project 'Sustainable Orphan Drug Development through registries and monitoring', the registration of metabolic diseases (www.DDRMD.nl), Treat NMD & CRAMP (both muscle diseases, www.isno.nl) or Eurocat (www.eurocatnederland.nl). In 2014, the European Commission will start setting up a platform for registrations of rare diseases. *What is missing:* Clinical drug research, which usually takes place more or less simultaneously in different countries, has not taken place in the Netherlands for a number of rare diseases. The pharmaceutical companies make their own decisions in which countries they will conduct the research. One reason that the Netherlands is not involved in some studies is the current regulations regarding the conduct of phase I research with children. Following the effectiveness study with the orphan drugs for Fabry disease and Pompe disease, there has been a need for an assessment framework that, even in research involving small groups of patients, can lead to insight into the added value of the treatment and thus decision-making about reimbursement of treatment. Attention should also be paid to research into the benefits of care and treatment, with attention to increasing life expectancy and quality of life. In the discussion about expensive care and treatment, such returns are still not sufficiently taken into account. The natural history of the disease is not sufficiently known for many patients with a rare disease. More knowledge about the natural course of the disease means that complications can be identified in time or even prevented and also provides a better starting point for research into the efficacy and effectiveness (efficiency and effective use) of new medicines. Genetic diagnostics could improve through more research into gene variants and making the research results accessible worldwide via databases. Basic scientific research in the Netherlands is of high quality, but the translation into clinical application or care requires improvement. Other suggestions for new research in the field of rare diseases are: cross-disease research into symptoms that occur in various rare diseases; research into options for early detection, diagnosis, screening, preconception care and prevention of rare diseases and research into the genetic components that play a role in rare diseases and the impact of rare diseases on daily life. Publications on rare diseases can contribute to increasing knowledge about rare diseases, in particular very rare diseases. Another aspect that deserves more attention is research into the use of medicines that are already on the market for the treatment of rare diseases (off-label use). Patient registers can help collect such research data, but this is still done too little and not on a structural basis. One of the reasons for this is the lack of uniform coding. The ICD-10 is often not suitable for coding rare diseases.63 Data on people with rare diseases is not kept over a longer period and often only nationally. Much research that involves registration is funded for a short period of time without any prospect of follow-up. A possible threat to (medical) scientific research is that government budgets for research are reduced or redistributed. This is possible have consequences for research into rare diseases. Moreover, there are insufficient financial resources for research over a longer period.

	Theme 5: Amplifying the voice of the patient with a rare disease Theme description: This theme relates to general advocacy and proactive action from the perspective of patients and their representatives in the broad field of life with a rare, often chronic disease. Patient organisations can play a role in all the themes described in the previous chapters: improving knowledge and information, drawing up care pathways, prioritizing research or identifying bottlenecks with regard to diagnostics, care and treatment. This theme also relates to the empowerment of patients with rare diseases. *What is already there:* There are various organisations for patients with a rare disease and parents where they can contact fellow sufferers, information and advice. In the Netherlands there are estimated to be approximately 350-400 disease-specific or categorical patient organisations. A number of these are a cluster of rare diseases or a collaboration, for example for muscle diseases, metabolic diseases, blood diseases, chromosome disorders. The government recognises a number of umbrella organisations and platforms that operate at a national level: the NPCF, CG Council, Platform VG and LPGGz. Only these umbrella organisations receive operating subsidies from the PGO Fund, part of the Ministry of Health, Welfare and Sport. For several years now, the VSOP has been the national contact point for rare diseases at the European umbrella organisation EURORDIS. The VSOP is a partnership of 66 affiliated organisations, most of them for rare and/or genetic disorders. Together with supporters and other patient organisations, the VSOP has a number of projects in the field of rare diseases. In the Netherlands, unlike other countries, subsidies (via the PGO Fund) are available for patient organisations. The government has decided to give patient and disabled organisations the space to realise bundling and cooperation themselves until 2015, partly with the use of vouchers. In 2015 it will be assessed whether progress has been made in joining forces. If this joining of forces is not sufficiently achieved, stricter subsidy conditions will be implemented. This can lead to a redistribution of available resources. Collaboration and joining forces is necessary for rare diseases, precisely because of the large number of diseases. A number of collaborative projects involving vouchers were started in 2013. A number in the field of rare diseases. An overview of these projects is included in the appendices. *What is still missing:* It is important to better structure general advocacy for people involved in rare diseases, which is currently fragmented. Due to the rarity of the diseases, there are a number of generic aspects that can play a role in the development of new legislation and regulations or in their implementation. The umbrella organisations for the chronically ill are insufficiently equipped to represent interests in the field of rare diseases, although they are consulted by the government. Solutions for bottlenecks and policy decisions for more common chronic diseases often provide no or insufficient solution for the specific situation of people with a rare disease. There is currently no complete overview of all patient organisations or contact groups that exist for rare diseases in the Netherlands. An additional problem is that there is often no Dutch patient or parent association for very rare diseases. Patients worldwide can find each other more easily with the help of the internet, but people with very rare diseases more often encounter problems in Dutch healthcare due to the unfamiliarity of the disease among healthcare providers, healthcare institutions, insurers and the government. An important condition for better organizing the voice of a patient with a rare disease is that the larger cross-disease and disease-specific patient organisations seek connections and are open to new members of their tribe. This creates more empowerment (effectiveness). It is still for very small groups or individuals. It is often not possible to join an association. Advocacy in general is under pressure due to changes in the financing of patient organisations (see 6.1). A number of advocacy initiatives are dependent on project subsidies, while advocacy should be a structural point of attention. Patient organisations have an important role in drawing up the NPZZ. At a meeting organised by the VSOP (in 2012), they expressed their wish to play a prominent role in the implementation and coordination of the NPZZ. However, there is no consensus yet within patient organisations on how this could be organised or achieved. **Theme 6: Direction and continuity**

	Direction: After the recommendations from the NPZZ concept were discussed in various meetings with field parties (hearing, conference) and within the sounding board group, attention was subsequently paid to the subject of management. In particular, this relates to the question: which organisation can be held responsible for activities arising from the plan? Who can monitor the coherence between different projects and activities, especially for aspects that do not fall under the responsibility of a field party or where it is necessary to keep an overview. Attention has also been drawn to a future evaluation of the objectives or outcomes of the plan and to the monitoring of activities that require continued attention. *What is already there:* The National (Dutch) Plan for Rare Diseases was presented to the Minister of Health, Welfare and Sport on October 10, 2013. In November 2013, the VSOP will organise a conference on the National Plan in the context of the EUROPLAN project. In its mission letter, February 2012, the Ministry of Health, Welfare and Sport requested the Biotechnology and Genetics Forum (FBG) to contribute to tackling the problems of people with a rare disease and, in this context, commissioned the plenary consultation between the relevant parties on to take. In particular, this concerns the position of the patient and the development of orphan drugs and, if necessary, advising the government on this. From Europe, the EUCERD will monitor the development of plans for rare diseases within Europe. The EUCERD has drawn up a document with 21 indicators that can be used to record data on the process and results of the national plan in each country. In 2013, several new projects in the field of rare diseases and orphan drugs were started, financed, among others, by the PGO Fund and by ZonMw. The first results of these projects are expected in 2014-2015. *What is still missing:* Various parties in the field have suggested that attention should continue to be paid to a European policy for rare diseases in addition to all national plans, especially for aspects where European cooperation and coordination is necessary, for example in the field of research. No budget has been drawn up for the implementation of the plan. In that sense, the plan is an impetus to undertake activities and the parties involved in the field have a task to ensure personnel and/or financial cover for the implementation of activities. The Ministry of Health, Welfare and Sport should make it clear where the (delegated) responsibility lies for directing the proposed actions. Various parties involved feel the need for a rare diseases coordination point where the knowledge acquired from the field is brought together, developed and further implemented. It is also noted that such a group must have support and be authoritative for making decisions. An independent/scientific or overarching coordination point is advocated. These include: Quality Institute, ZonMw, RIVM, University or Health Insurers.
Targets (if specified) and measurement method(s) (where available)	*None mentioned.*
Implementation action(s), lead(s) and key performance indicator(s)	**Note: The strategy does not describe activities for individual situations or for individual rare diseases.** **Theme 1: Unfamiliarity with rare diseases** Recommendations: ▪ Encourage increasing general awareness of 'the phenomenon' of rare disease among healthcare and care providers, health insurers, (umbrellas of) patient organisations, policy maker in government and municipalities and the general public. ***1st point of contact*** *(other parties)*: **VSOP** (in collaboration with CG Council and NPCF Rare Disease Fund) ▪ Increase alertness to rare diseases among primary care doctors, doctors in training as specialists and in the further training of medical specialists. Make education about rare disease explicit in the medicine curriculum (Framework Plan), for specialists in training and in further training of specialists. ***1st point of contact*** *(other parties)*: **Framework plan for training doctors (NFU)** (in collaboration with scientific associations).

Theme 2: Information provision and communication
Recommendations:

- Improving differential diagnosis of rare diseases by: a) Use of ICT: e-learning and other ICT applications; b) Use of e-mail and video consultation from the expertise centre; c) Improving visibility of rare diseases (general) and information about centres of expertise.
  1st point of contact *(other parties)*: **NFU/STZ** (Patient organisations and health insurers).
- Knowledge about the symptoms of rare diseases and the instruments for diagnosing rare diseases must improve in primary and secondary care.
  1st point of contact *(other parties)*: **NHG and AJN (and NCJ)** (in collaboration with other scientific associations).
- Portal website and counter and referral function for: People looking for a diagnosis; Patients and/or parents/family who are looking for information about the disease, (genetic) research, fellow sufferers, a patient organisation or expertise centre; Care providers, students or teachers looking for general information about (the support of people with) rare diseases; Systematic collection of information from the group of patients with rare diseases (and their parents).
  1st point of contact *(other parties)*: **Erfocentrum** (In association with Orphanet and VSOP).
- Improving overall access to information about rare diseases in understandable language for patients, families and referrers.
  1st point of contact *(other parties)*: **Erfocentrum** (and Orphanet in collaboration with NFU (TRF portal).
- Desk or reporting point for people who have problems with care or reimbursement of treatment (signalling function for advocacy).
  1st point of contact *(other parties)*: **VSOP** (in collaboration with CG Council and NPCF).
- Make an overview of all organisations in the Netherlands patients and parents involved in rare diseases.
  1st point of contact *(other parties)*: **PGO support** (in collaboration with VSOP CG Council and NPCF)
- Scientific associations, professional groups and patient organisations regularly organise symposia or further training on various aspects of rare diseases.
  1st point of contact *(other parties)*: KNMG, KNMP, NHG, VenVN, patient organisations, FBG. At European level EURORDIS or EPPOSI.

Theme 3: Organisation of care and availability of therapy
Diagnostics Recommendations:

- Improve alertness to rare diseases.
  1st point of contact*:* **VSOP**/in collaboration with CG Council and NPCF Rare Disease Fund; **Framework plan for training doctors (NFU)** (in collaboration with scientific associations); **NFU/STZ** (Patient organisations and health insurers); **NHG and AJN (and NCJ)** (in collaboration with other scientific associations)
- It must be periodically examined whether the number of diseases included in the heel prick test can be expanded based on new insights. The heel prick accelerates timely diagnosis of rare diseases.
  1st point of contact *(other parties)*: **VWS**
- Research into whether screening options (for example cascade screening) can be used for the detection of hereditary rare diseases.
  1st point of contact *(other parties)*: **FBG** (VKGN, STOET (foundation for the detection of hereditary tumours))
- There needs to be more attention and information about the genetic aspects of rare diseases.
  1st point of contact *(other parties)*: **VKGN** (in collaboration with the Erfocentrum)

Organisation of Care Recommendations:

- Bring expertise centres for rare diseases under the Wbmv.
  1st point of contact *(other parties)*: **VWS**

	▪ Designate expertise centres in a transparent manner using existing uniform criteria. ***1st point of contact*** *(other parties)*: **VWS** ▪ Directors are responsible for the adequate functioning of expertise centres over a longer period of time. ***1st point of contact*** *(other parties)*: **Guessing management of UMCs** ▪ Expertise centres work with multidisciplinary teams for children and adults with rare diseases with a point of contact (care coordinator). Attention is paid to the transition of care from child to adult. ***1st point of contact*** *(other parties)*: **NFU** (in collaboration with STZ) ▪ Expertise centres contribute to the development of care standards and guidelines and work in accordance with the established procedures of this standard. ***1st point of contact*** *(other parties)*: **NFU** (in collaboration with STZ and VSOP) ▪ More attention should be paid to the NHG standard preconception care. ***1st point of contact*** *(other parties)*: **NHG** ▪ More attention should be paid to preconception genetic counselling (FBG identification) If necessary, carry out a pilot that provides more insight into the possibilities and possible bottlenecks. ***1st point of contact*** *(other parties)*: **VWS** (FBG) ▪ Care close to home ('care in the neighbourhood') should be better coordinated in consultation with the expertise centre. ***1st point of contact*** *(other parties)*: **LHV** ▪ Develop a 'rare diseases' code (morbus rare) or use the 'Orphacode' (Orphanet). ***1st point of contact*** *(other parties)*: **RIVM** ((ICD/ICF) in collaboration with NHG (HIS), NFU (ZIS), Orphanet (Orphacode),VKGN (Cineas) ▪ Setting up and maintaining a database with data on people with rare diseases must become a billable presentation. A patient does not always have to come to the centre, they can also collaborate with hospitals in the region with the help of ICT. For example e-Health. ***1st point of contact*** *(other parties)*: **NZa**, Health insurers and DBC maintenance ▪ People with a rare disease often see various specialists, who often repeat examinations, such as taking photos or blood tests. Patients find this burdensome and often it has no added value. There is a need for coordination of care. ***1st point of contact*** *(other parties)*: **ZN and Health insurers** **Availability of Treatment** Recommendations: ▪ When developing the policy regarding reimbursement for orphan drugs, specific features of the treatment of rare diseases (small groups of patients, great diversity) must be taken into account. ***1st point of contact*** *(other parties)*: **VWS** ▪ Research into the natural history and into start and stop criteria, dose and frequency can provide information about the effective use of orphan drugs. ***1st point of contact*** *(other parties)*: **NFU** (and UMCs Nefarma and Biofarmind CVZ) ▪ Research and data collection is necessary regarding the off-label use of medicines for rare diseases, so that they can be reimbursed - after positive advice from CVZ. ***1st point of contact*** *(other parties)*: **UMCs** (CVZ and Health Insurers) ▪ Purchasing care in line with designated expertise centres for rare diseases. Rare diseases are declared non-competitive (introduction of limited contracting for expertise centres). ***1st point of contact*** *(other parties)*: **ZN** and Health Insurers ▪ Implement legislation in the Netherlands in the field of cross border care.

	1st point of contact *(other parties)*: **VWS** ▪ Introduction of chain care (Chain DBC) for rare diseases, analogous to Pilot CF ***1st point of contact*** *(other parties)*: **ZN, Health Insurers** (and Quality Institutes) **Theme 4: Research** Recommendations: ▪ Improve instruments for signalling and recognition of rare diseases from general practice and youth healthcare. ***1st point of contact*** *(other parties)*: **NHG and NCJ** ▪ Increase the awareness and findability of rare diseases in literature by including the term rare disease or Orphan or Rare Disease in the text of the scientific article, also as a search term. ***1st point of contact*** *(other parties)*: **Scientific Associations** (NFU and STZ) ▪ The scientific research field must pay continued attention to: - medical and social scientific aspects of rare diseases; - the development of more and better diagnostic methods; - (new) therapeutic options for rare diseases natural history of rare diseases efficiency and cost-effectiveness research of orphan drugs. ***1st point of contact*** *(other parties)*: **ZonMw** (in collaboration with SGF and NFU, Nefarma and Biofarmind) ▪ Encourage research into treatment with existing medicines that are not (yet) registered for the disease (off label application). ***1st point of contact*** *(other parties)*: **ZonMw NFU** (UMCs, Nefarma and Biofarmind) ▪ More research into improving genetic diagnostics for more rare diseases (including exome and genome sequencing) and research into gene variants and publication of this data in global databases. ***1st point of contact*** *(other parties)*: **VKGN** ▪ Subsidy rare disease research in which different scientific disciplines (for example medical and social sciences) collaborate nationally and internationally. ***1st point of contact*** *(other parties)*: **ZonMw/E-Rare** ▪ Involve patients in setting priorities in new research programs, determining endpoints, mapping natural history, quality of life research and in research into palliative care for rapidly progressive diseases. ***1st point of contact*** *(other parties)*: **ZonMw** (in collaboration with NPCF, SGF and VSOP) ▪ International research is needed into new (HTA and MTA) methods for measuring the effectiveness and efficiency of orphan drugs. ***1st point of contact*** *(other parties)*: **ZonMw** ▪ Encourage public-private partnerships for the development of therapy. ***1st point of contact*** *(other parties)*: **ZonMw** (in collaboration with the SGF, Nefarma and Biofarmind) ▪ Develop and finance a follow-up database (NEORAH) for all rare diseases in the heel prick for long-term research into the course of the condition. ***1st point of contact*** *(other parties)*: **VWS and RIVM** ▪ Registries and biobanks should be an integral part of Dutch expertise centres for rare diseases and should, as far as possible, connect with registrations in other countries. In addition, the maintenance of a patient register/database of people with rare diseases must be funded. ***1st point of contact*** *(other parties)*: **NFU and ZN** ▪ Concentrate specific scientific research for those (groups of) rare diseases for which the centre already has expertise. Build on research, clinical excellence and innovation. ***1st point of contact*** *(other parties)*: **NFU**

	▪ Remove barriers to the development of new diagnostic tools and new therapies for rare diseases. Expand legal restrictions included in the WMO for conducting phase 1 and phase 2 research in children. ***1st point of contact*** *(other parties)*: **VWS (law amendment)** CCMO and METCs (implementation) **Theme 5: Strengthening the voice of the patient with a rare disease** **Recommendations:** ▪ Increasing and expanding cooperation between patient organisations regarding generic aspects of rare diseases, especially for the purpose of advocacy, is necessary. ***1st point of contact*** *(other parties)*: **VSOP** (in collaboration with CG council and NPCF) ▪ Patient organisations must be encouraged to connect fellow sufferers or small groups (clustering per disease group) and to collaborate more in the field of rare diseases. ***1st point of contact*** *(other parties)*: **PGO Fund** (in collaboration with NPCF) ▪ Patient organisations and health insurers must work together more closely. This will stimulate the development of care pathways and care chains and improve the quality of care and purchasing of care for people with rare diseases. ***1st point of contact*** *(other parties)*: **VSOP** (in collaboration with CG council, NPCF and Health Insurers) **Theme 6: Direction and continuity** **Recommendations:** ▪ A director must be appointed who has primary responsibility for implementing the plan and initiating activities in the plan. ***1st point of contact*** *(other parties)*: **Minister of Health, Welfare and Sport** ▪ There is a need for a government advisory body that closely monitors the activities in the plan, monitors and reports on progress and bottlenecks. ***1st point of contact*** *(other parties)*: **FBG** **<u>Prioritised Recommendations</u>** *Urgent/ short term (desired start next year 2014):* ▪ Appointing a director for the entire plan ▪ Clarity regarding policy for expertise centres and EU reference centres, mainly in the context of the Cross-border Care Legislation ▪ Promote timely and adequate diagnostics and promote alertness and knowledge about rare diseases or data regarding natural history. This also stimulates the development of a care chain *Medium term (starts in 2 to 3 years):* ▪ Designation of centres based on uniform criteria, the presence of multidisciplinary chain care and care pathways ▪ Coordination and coordination of care and sharing of information (shared care and chain care) ▪ Adequate financing of care (DBC chain) ▪ Follow-up funding for ongoing research programs in the field of rare diseases and orphan drugs *Longer term (3 years or longer): Recommendations that will take a longer time to implement and/or for which it is currently unclear how (and when) these activities could start.* ▪ Financing new research/new programs regarding rare diseases (medical-scientific, social scientific)

	▪ Adequate and uniform coding and national registration of rare diseases ▪ Long-term research into the natural course of the disease, early treatment options and measures to prevent and treat complications ▪ Development of new therapies by Dutch researchers and companies ▪ Evaluation of activities and returns of the plan (NPZZ) *Ongoing attention: There are a number of aspects that require continued attention, which do not benefit from a project based approach where the attention fades away after the end of the project. This concerns aspects such as:* ▪ Input from patient (organisations) in policy making and setting priorities strong advocacy for rare diseases ▪ Adequate education and training of healthcare providers and care providers with regard to rare diseases ▪ Knowledge and education, early detection and alertness for rare diseases ▪ Infrastructure for collecting knowledge about rare diseases and maintenance databases ▪ Entitlement to and financing of adequate treatment of rare diseases
Governance and organisational structures	This strategy contains elements for which the government is responsible, such as prevention and early detection (screening) of diseases in newborns and such as the financing of orphan drugs. The strategy also outlines the requirement to appoint a director/coordinator for the above recommendations to promote coherence and help prevent fragmentation and unnecessary duplication. Additionally, each individual recommendation names one party that should take primary responsibility. The action plan tries to encourage these parties to feel responsible for the recommendation and to encourage action to be taken. Most recommendations also include suggestions for organisations with which to collaborate on the action point/recommendation.
Funding model	The Ministry of Health, Welfare and Sport has not allocated a budget for proposed measures and activities to this plan. Of course, recommendations are also made that do not have to cost extra money. These recommendations relate to a different approach within existing structures/organisations.
References and or links to other initiatives	
Screening programmes (including newborn screening)	*See diagnostics (What is already there) and recommendation - Research into whether screening options (for example cascade screening) can be used for the detection of hereditary rare diseases. The policy regarding heel prick remains unchanged and youth healthcare carries out screenings for children with established guidelines (see summary of the Ministry of Health, Welfare and Sport strategy).*
Personalised medicine, genomics, genetic counselling	*See diagnostics which identifies that new methods of genetic diagnosis are not well used and recommendation - There needs to be more attention and information about the genetic aspects of rare diseases.* *See organisation of care which identifies recommendation - More attention should be paid to preconception genetic counselling (FBG identification) If necessary, carry out a pilot that provides more insight into the possibilities and possible bottlenecks.* *See Research which identifies recommendation - More research into improving genetic diagnostics for more rare diseases (including exome and genome sequencing) and research into gene variants and publication of this data in global databases.*
Models of care/care pathways	*See Theme 3 - Organisation of care and availability of therapy.*

	See Medium term recommendations - Designation of centres based on uniform criteria, the presence of multidisciplinary chain care and care pathways. *See Theme 5 Strengthening the voice of the patient with a rare disease and recommendation - Patient organisations and health insurers must work together more closely. This will stimulate the development of care pathways and care chains and improve the quality of care and purchasing of care for people with rare diseases.*
Workforce	*See unfamiliarity with rare diseases and recommendation - Increase alertness to rare diseases among primary care doctors, doctors in training as specialists and in the further training of medical specialists. Make education about rare diseases explicit in the medicine curriculum (Framework Plan), for specialists in training and in further training of specialists.* *See ongoing attention recommendation – Adequate education and training of healthcare providers and care providers with regard to rare diseases.*
European Reference Network	*No mention of European Reference Network.*
EU alignment and participation	During the Council of Ministers of Health of the EC (Luxembourg 2009), the Netherlands endorsed The European RECOMMENDATION of the Council of Ministers of the European Union (8 June 2009). The Netherlands, like all other Member States, has therefore taken on the obligation to draw up a plan or strategy by 2013 at the latest that will serve as a guideline for and structure all relevant measures in the field of rare diseases, in the context of its health and social system.
Health information (including rare disease registries)	*See Theme 2 Information provision and communication.* ***Specifically registries*** *See research and recommendation - Registries and biobanks should be an integral part of Dutch expertise centres for rare diseases and should, as far as possible, connect with registrations in other countries. In addition, the maintenance of a patient register/database of people with rare diseases must be funded.* *Also see longer term recommendation - Adequate and uniform coding and national registration of rare diseases.* *From the strategy of the Minister of Health, Welfare and Sport see Registration of rare diseases (additional information).*
Orphan medicines	Heavily referenced throughout. For specifics see: Theme 2: Care and availability of treatment – Availability of orphan drugs. Recommendations - When developing the policy regarding reimbursement for orphan drugs, specific features of the treatment of rare diseases (small groups of patients, great diversity) must be taken into account. - Research into the natural history and into start and stop criteria, dose and frequency can provide information about the effective use of orphan drugs. See Research and recommendations - The scientific research field must pay continued attention to efficiency and cost-effectiveness research of orphan drugs.

	- International research is needed into new (HTA and MTA) methods for measuring the effectiveness and efficiency of orphan drugs. See Urgent/short term recommendation - Consistent policy regarding entitlement and reimbursement of orphan drugs. See Medium term recommendation - Follow-up funding for ongoing research programs in the field of rare diseases and orphan drugs. See strategy of the Minister of Health, Welfare and Sport – Reimbursement of orphan drugs - From 2014 (postponed to 2016), orphan drugs will only be funded through hospital financing. This transfer has no influence on the entitlement.
Rare disease research	The strategy refers to various projects in the field of rare diseases. In this appendix you will find an overview of projects that have received financing for the implementation of their project, started in 2012 or 2013 and in which different organisations and different field parties, public and private, national or international, collaborate. In addition, there are many other initiatives or projects in preparation that may be important for rare diseases, but these are not included in the current overview. We have also not included projects by individual patient organisations for specific groups of rare diseases in this overview. Most of the projects below will end in the period 2014-2015. It goes without saying that the proceeds from these projects can be used in drawing up the next National Plan, with new priorities. **Projects by patient organisations in collaboration with other patient organisations or other partners (financed by the PGO Fund or Innovation Fund)** **Project Name:** Expertise in rare disorders from patients perspective **Objective/overview of project activities:** The aim of the project is to map knowledge about a number of rare diseases by visiting a number of expertise centres. The basis for this is a list of criteria that expertise centres should meet according to the project partners. www.expertiseinkaart.nl **Participants/Partners:** VKS in collaboration with Pulmonary Fibrosis Patient Association, Klub van Lange Mensen, PKU association, Vasculitis Foundation, Association Nee-eten. **Timeline:** 2013 **Project Name:** Standards of Care for Rare Conditions **Objective/overview of project activities:** The project aims to develop 16 standards of care for rare Conditions (www.zorgstandarden.net). **Participants/Partners:** VSOP in collaboration with patient organisations with which a standard of care is developed. **Timeline:** 2012 -2014 **Project Name:** Heard, seen and known. Innovation through participation in policy for people with uncommon conditions **Objective/overview of project activities:** This project includes: an annual policy symposium on implementation of the National Plan for Rare Diseases; a Multi-stakeholder Platform (Madurodam Group); Working Group on Genetics, Pregnancy and Ethics; the organisation of the annual Rare Diseases Day. And developing a contact point, consisting of a signpost and a portal. **Participants/Partners:** VSOP in collaboration with AIS Netherlands, CMTC-OVM, Dit Koningskind, Helping Hands, HMEMO association, Youth Rheumatism Association Netherlands, NPV, Contact Group AA & PNH, Association Tietze and costochondritis patients, FSIGN, Ehlers Danlos Patients, SCCH **Timeline:** 2013-2015

	Project Name: Innovation through participation in quality of care and prevention for people with uncommon conditions **Objective/overview of project activities:** This project includes: Updating and expanding the healthcare standards website; improving primary care (particularly general practitioner care) by promoting and implementing the 'patient as information carrier' brochures and developed care standards for rare diseases. In addition, developing care advice and developing a user version of care standards. **Participants/Partners:** VSOP in collaboration with Paget, Fragile X, NFVN, SAS, VSN, HCHWA-D, Spinal Cord Injury NL, Adrenal Association, NVACP, SCCH. **Timeline:** 2013-2015 **Project Name:** Patient in perspective. Participation in healthcare research and therapy development for people with uncommon conditions **Objective/overview of project activities:** This project includes: Date to innovate (annual meeting for patients, researchers and medical product developers); alerting patient organisations (particularly partners) to subsidy opportunities; participation in the working group on medical scientific research and medical databases; and the child and illness working group. An exploration of healthcare research and therapy development and patient-driven registries. **Participants/Partners:** VSOP in collaboration with the Child and Hospital Foundation; HCHWAD: HEVAS, DES Foundation, Noonan Syndrome Foundation, Association of Allergy Patients, Association of older incubator children; Galactosaemia Association, NL Association for Haemophilia Patients. **Timeline:** 2013-2015 **Project Name:** Mentally disabled: care in the future **Objective/overview of project activities:** The aim of this project is to develop the care module: transition for people with an intellectual disability. **Participants/Partners:** VSOP in collaboration with: PlatformVG, UMC St. Radboud Nijmegen, Maastricht University Hospital, Elkerliek Hospital Helmond, Amphia Hospital Breda, Maasstad Hospital Rotterdam and Rotterdam University of Applied Sciences. **Timeline:** 2013-2015 **Project Name:** Amplifying the patient's voice **Objective/overview of project activities:** The aim of the project is to set up an information provision analogous to the Medical Home Portal/Chronic care model. An important element of the portal is early detection and diagnosis. Patient organisations and experts will provide information to promote timely diagnosis in primary care (the clinic, general practitioner and general specialist). A design for connection with the Digital Child File is made, so that after the diagnosis, the information from before the diagnosis can be used to promote early recognition. **Participants/Partners:** Perspective Foundation in collaboration with: Mentally disabled: care in the future Shwachman Support Holland Foundation, Oscar Netherlands, Sarcoidosis Interest Association Netherlands, FOP Netherlands Foundation, Rubenstein Taybi Foundation, Perspectief Foundation, Laposa Foundation, Dutch association for hereditary angioedema and Quincke's oedema, Marshall Smith Syndrome Research Foundation, Legionnaires' Disease Foundation, Association of Parents of SIDS Children. **Timeline:** 2013-2015 **Project Name:** Care pathway for Neuro-Muscular Disorders (NMA).

	Objective/overview of project activities: Setting up a multidisciplinary NMA care path, aimed at quality of life with an NMA, the patient's desired interpretation of life by strengthening the patient's own control. The targeted coordination between healthcare providers, patients and healthcare providers/informal caregivers. **Participants/Partners:** UMC St. Radboud, RMC Groot Klimmendaal and Sisa, Association of Muscular Diseases Netherlands (VSN). **Timeline:** Started in 2013 **<u>Projects within the ZonMw program Priority Medicines for rare diseases (PM Rare)</u>** **Project Name:** Antisense therapy for several major rare diseases. **Objective/overview of project activities:** Duchenne's disease. The researchers are trying to make the defective gene function better through so-called exon skipping. We are investigating whether this method works in collaboration with Prosensa and GlaxoSmithKline. In addition, it is being studied whether exon skipping can also be applied to Huntington's disease and CADASIL. **Timeline:** 2012-2016 **Project Name:** Gene-corrected stem cells for curative treatment of SCID. **Objective/overview of project activities:** This research focuses on the immune disorder Severe Combined Immunodeficiency (SCID). Children with this condition lack white blood cells, which are crucial for a good immune system. They can be treated with bone marrow transplantation. They want to treat these patients with gene therapy. **Timeline:** 2012-2016 **Project Name:** Towards treatment of MELAS syndrome: drug development based on newly identified compounds. **Objective/overview of project activities:** The grant supports research into new treatment methods for MELAS syndrome, a rare hereditary metabolic disease. To carry out this research, a multidisciplinary team has been formed consisting of public and private parties. For 5 years, Mercachem, Khondrion and the UMC St. Radboud will contribute their expertise to develop a treatment. **Timeline:** 2012-2016 **Project Name:** Treating the cognitive deficits associated with NF1 using the HCN channel agonist lamotrigine. **Objective/overview of project activities:** Children with the condition Neurofibromatosis type 1 (NF1) often also have problems with learning, concentration or behaviour. Researchers from Erasmus MC have found the cause of these problems in mice with an NF1 mutation. If the mice are given a drug (lamotrigine) that stimulates the HCN channel, the brains function normally again and the learning problems are resolved. To test whether Lamotrigine can also help children with NF1, the researchers will conduct a clinical trial. **Timeline:** 2013-2015 **Project Name:** A novel technology to improve Enzyme Replacement Therapy for Mucopolysaccharidosis I and Fabry disease. **Objective/overview of project activities:** The proposed project will focus on studies in cell cultures and in relevant mouse models, to provide a proof-of-principle that GSHPEG liposomes containing lysosomal enzymes leads to better clearance of accumulated substrates in the clinically relevant tissues as compared to unshielded enzyme. The AMC, with its clinical and laboratory expertise on LSDs, combined with to- BBB's experience in generating GSH-PEG liposomes containing drugs and their knowledge on targeting the brain, will create the optimal platform for this study. Collaboration with the Stem Cell & Neurotherapies Lab in Manchester provides essential expertise for this project on MPS I brain pathology in the mouse model and on antibody studies in MPS.

	Timeline: 2013-2015 **Project Name:** Thyroid hormone analogue therapy of patients with severe psychomotor retardation caused by mutation in the MCT8 thyroid hormone. **Objective/overview of project activities:** Thyroid hormone is important for normal brain development and metabolism. Patients with mutations in an important thyroid hormone transporter (MCT8) have severe intellectual disability and abnormal thyroid hormone levels. The aim of this research is to reduce or prevent the serious consequences of this disease by: restoring the functioning of thyroid hormone at the cellular level and normalizing abnormal thyroid hormone levels. The researchers hope to achieve this by administering a substance derived from thyroid hormone to these patients. This substance is absorbed by the cell via a different route than via MCT8 and mimics the action of thyroid hormone. **Timeline:** 2013-2015 **Project Name:** Preventing arrhythmias and sudden cardiac death in long QT syndrome type 3 through pharmacological late sodium current inhibition. **Objective/overview of project activities:** Long QT syndrome type 3 (LQT3) is a rare genetic disorder caused by mutations in the SCN5A gene encoding the cardiac sodium channel, and is characterised by prolonged QT intervals on the ECG, and increased risk for sudden death due to ventricular tachyarrhythmias, in particular torsades de pointes. Compared to other LQT subtypes, LQT3 patients are particularly at risk for sudden death, and cardiac arrest (rather than syncope) is often the first clinical event. Pharmacological treatment options for LQT3 are limited. At the moment, high risk LQT3 patients are treated with implantation of an implantable converter defibrillator (ICD), often in combination with beta blockers ICD implantation however has serious complications and tremendous impact on quality of life. **Timeline:** 2013-2015 **Project Name:** Orphan information Point medicines **Objective/overview of project activities:** The Orphan Drug Advice Centre will serve as a portal for research and business, bundling expertise in the field of research and development of new therapies (orphan drugs) for rare diseases. This new advice point will be a valuable source of information for applied research, companies and others, with the ultimate goal of accelerating the flow from research to the patient. **Timeline:** 2012-2013 **Projects with Dutch researchers that were funded within the European E-Rare project in 2012** **Acronym:** CURE-FXTAS **Title:** Experimental approaches towards therapeutic intervention for Fragile X-associated Tremor Ataxia Syndrome **Acronym:** SpliceEB **Title:** Splicing therapies for Dystrophic Epidermolysis Bullosa **Acronym:** TARGET CdLS **Title:** Targeting unknowns in causes and phenotypes of the Cornelia de Lange Syndrome

	Acronym: PPPT-MJD **Title**: Towards the understanding of pathological protein processing and toxicity in Machado-Joseph Disease **Acronym**: Eur-USH **Title:** European young investigators network for Usher syndrome **Acronym:** ALS degeneration **Title:** The molecular basis for neurodegeneration and muscle atrophy in ALS **Acronym:** HEART DM **Title:** Exploring the mechanisms of heart dysfunctions in myotonic dystrophies **Acronym**: PYRAMID **Title**: Phenotype Research for ALS modifier discovery **Acronym:** EMINA-2 **Title:** European Multidisciplinary Initiative on Neuroacanthocytosis –2 **Acronym:** COQ-iPSC **Title:** Deficiency Syndrome: Understanding the genotype-phenotype association and metabolic dysfunction through generation of induced pluripotent stem cells from patient-specific uncorrected and genetically-corrected cells **Acronym:** EuroDBA **Title:** European Diamond-Blackfan Anaemia Consortium
Alignment beyond the healthcare sector	*Nothing specific mentioned.*
Any additional information (for example, background to the strategy or strategy development)	Strategy development: The Orphan Drugs Steering Group (until December 31, 2011) and subsequently the ZonMw national rare disease strategy Sounding Board Group supervised the preparation of the plan. A website was set up (www.npzz.nl) with information about various activities in the field of rare diseases. Previous versions were released for consultation via this website. In addition, various working groups and field parties contributed or commented on draft versions. The National Plan for Rare Diseases (NPZZ) has been drawn up under the responsibility of ZonMw, which has set up an NPZZ Sounding Board Group for this purpose (2012-2013). The sounding board group met five times about the plan. Summaries of the meetings have been published on the NPZZ website. For the purpose of public consultation, three versions of the plan have been published via the website (www.npzz.nl). Many individuals and organisations have contributed to the plan. Below is a chronological overview of the steps taken to arrive at a final version of the plan:

	▪ The themes of counter, information, care, treatment, research, availability of therapy, and availability of knowledge were discussed separately and in depth in the NPZZ sounding board group (2012-2013). ▪ The same themes were discussed in multidisciplinary working groups (meetings at the end of 2011 and a written round at the beginning of 2013) and in a Hearing (April 2012). ▪ The first version of the NPZZ was presented and discussed at a public meeting and on the website www.npzz.nl posted (August 2012). ▪ The second version was published on January 29, 2013 on www.npzz.nl. ▪ The comments were collected and discussed at the meeting of the NPZZ sounding board group in March 2013. ▪ The second version of the NPZZ was adjusted following this meeting, which was followed by a round of comments within the sounding board group (April-May 2013). ▪ The third version of the NPZZ was published on the website www.npzz.nl (May 2013). ▪ The third version was discussed by the Executive Board of ZonMw (May 2013). ▪ The comments on the third version were collected and discussed at the meeting sounding board group (June 2013). ▪ The NPZZ has been adjusted based on the comments and a final round of comments within the NPZZ sounding board group took place (June-July 2013). ▪ The final version of the plan including editorial adjustments has been drawn up (August - September 2013). ▪ The NPZZ was offered by ZonMw to the Ministry of Health, Welfare and Sport (October 2013). The composition of the sounding board and the individual and organisations involved in the development of the strategy were not extracted, as not deemed relevant. However they are outlined in the document. **Strategy of the Minister of Health, Welfare and Sport** This strategy was drawn up in addition to the strategy of the Minister of Health, Welfare and Sport (2012). The strategy of the Ministry of Health, Welfare and Sport (29 February 2012) regarding rare diseases discusses the policy of recent years and the current situation in more detail73. The government's influence is mainly possible in general areas such as accessibility, quality and affordability of care. The government can also help solve certain specific problems with the help of subsidies to targeted parties. However, government policy has no direct influence on the individual relationship between a patient with a rare disease and the healthcare providers or the healthcare institution. The strategy for the coming years will be partly continued, partly changed. The strategy for the coming years indicates that a number of tasks have been assigned to ZonMw and the Biotechnology and Genetics Forum. Other aspects of the government's national strategy are largely a continuation of current policy and relate to: *Diagnosis and treatment:* Diagnosing and treating a patient is considered top clinical or top referral care. The financial resources that the Ministry of Health, Welfare and Sport makes available through the academic component are intended for financing top referral care (80% care) and 20% is intended for research and innovation. Designating centres by the government is not an option in the short term. *Involvement of patient organisations:* Patient organisations are involved through representation in the NPZZ sounding board group and consultation, among other things, via the website of the National Plan; and through representation in the Biotechnology and Genetics Forum (FBG). Patient organisations receive financial support from the government via CIBG/PGO Fund.

	Screening: The policy regarding heel prick screening is expected to remain unchanged. Youth healthcare systematically carries out screenings for almost all children in accordance with established guidelines. The Foundation for the Detection of Hereditary Tumours (STOET) registers families with a predisposition to hereditary tumours and receives a subsidy from the Ministry of Health, Welfare and Sport. *Research:* The government finances scientific research through the Academic component, ZonMw programs and EU Framework programs. *Reimbursement of orphan drug* Other aspects of the government's national strategy are largely a continuation of current policy and relate to: From 2014 (postponed to 2016), orphan drugs will only be funded through hospital financing. This transfer has no influence on the entitlement. *Registration of rare diseases:* The government recognises that this is a difficult point and is not optimal. The government points to the European database for cancer, such a database could serve as the basis for a general registration system. *Involvement in European policy:* A representative of VWS sits on the EUCERD (European Committee for Experts on Rare Diseases).

Note: See abbreviation list in Themes or Priorities. The information in this table was extracted from a version of the original document translated to English using Google Translate.

Table B18. Data extracted for the Netherlands (Final Advice)

The Netherlands	Strategy information
Author(s) **Title**	ZonMw Final advice: Coordination meeting Rare Diseases[53] (Note: For further background information on these recommendations, see Appendix to the Final advice document).[54]
Timeline	Published 28 February 2017.
Overall aim(s)	The aim of the coordination meeting was to discuss: ▪ implementation of recommendations from the NPZZ ▪ bottlenecks regarding implementation ▪ making an inventory of new developments or identifying white spots ▪ coordination between the various parties that carry out activities or projects in the field of rare ▪ diseases and orphan drugs ▪ bundling 'loose' recommendations into coherent action points. The final advice from the Rare Diseases Coordination Consultation was drawn up on behalf of the Ministry of Health, Welfare and Sport. The basis for the coordination consultation is the National Plan for Rare Diseases from 2013. The final advice provides an update of the state of affairs of the NPZZ. In addition, it offers a look at future policy in the field of rare diseases and orphan drugs.

Themes and or priorities	**Good examples**
	Positive examples of initiatives are noted in the following areas:
	▪ Diagnostics
	  ○ Preconception care
	  ○ Next Generation Sequencing
	  ○ Genetic disorders
	▪ Information provision
	  ○ Information for patients and families
	▪ Early detection
	▪ Registration of rare diseases
	
	The coordination meeting identified a number of white spots that they believed did not have enough attention in the original National Rare Diseases strategy 2013:
	
	<u>Medical and social domain</u>
	The emphasis of the NPZZ 2013 was mainly on the medical (curative) domain. Too little attention has been paid to the connection with daily life, such as the domain of living, working, learning or leisure. Most rare diseases occur in childhood, are chronic, often progressive and are often accompanied by a physical and/or mental disability/disability. Rare diseases have a major impact on the daily lives of patients and their environment: parents, brothers and sisters, loved ones and informal caregivers. The unfamiliarity with rare diseases leads to misunderstanding in the immediate environment, causing problems in municipalities (for example with the provision of aids or adjustments), schools, work (inspection) and social integration and income or transport. An example of a bottleneck is the shift of care

	tasks to parents, who have to come to school to care for their children, in addition to their daily care tasks and work, due to the change in the financing of special education. Due to the unfamiliarity with rare diseases, many parents and children encounter misunderstandings regarding (intellectual) disabilities or abnormal behaviour. **<u>(Medical) expertise outside the centres</u>** The NPZZ has found that general practitioners and paediatricians have insufficient experience and expertise to identify rare diseases at an early stage. General practitioners and youth doctors have focused on this in the recent period. The recognition (correct/incorrect) of rare diseases certainly still deserves attention and can be greatly improved. In the description 'Early detection of rare diseases' of the Biotechnology and Genetics Forum, the youth doctor has an important role to play in (early) diagnosis. A number of other domains have been specified where there is insufficient knowledge about rare diseases. Mentioned are emergency care, occupational health and safety services and medical examiners, (special) education, municipalities, nursing home care and long-term care.
Targets (if specified) and measurement method(s) (where available)	*None mentioned.*
Implementation action(s), lead(s) and key performance indicator(s)	Note: In the Appendix document (Appendix A), how the coordination group mapped the status of the recommendations from the original strategy is presented. These are either red: has priority needs action; white sports: a missing theme or topic in the strategy; orange: ongoing monitor's progress; and green: ongoing, has been completed, or does not require action. The most important recommendation of the coordination consultation concerns the development of policy with which care (coordination), knowledge transfer and research are concentrated in the recognized expertise centres (recommended and implemented following the national rare disease strategy 2013) and can be expanded through their network for the benefit of people with rare diseases. In short, the recommendations from the coordination meeting relate to: ▪ care networks with expertise centres (also think of European reference networks) as a 'spin in the game' web' with specific attention to the (psycho)social domain ▪ policy regarding monitoring and evaluation of expertise centres ▪ financing of (chain) care/shared care and healthcare purchasing ▪ financing coordination of care, preferably at patient or family level ▪ financing of treatment, including (orphan) drugs ▪ uniform coding, national registration of core patient data; serves for this purpose funding ▪ financing long-term research programs for rare diseases, both nationally and internationally, aimed at pathogenesis and (psychosocial) treatment ▪ quality standards for rare diseases ▪ infrastructure for collecting and sharing knowledge, sustainable use of eHealth and ICT options in healthcare ▪ structural input and financing of the contribution of patients (organisations) and stimulation of national and international exchange of knowledge and experience among organisations of people with rare diseases ▪ coordinating network for monitoring. The recommendations are broken into: **1. Direction and Continuity, role for the government**

	2. Coordination, networking **3. Improving the quality of care** **<u>Direction and Continuity, role for the government</u>** The direction for national policy regarding the powers and responsibilities of expertise centres lies primarily with the Ministry of Health, Welfare and Sport. By implementing policy and enabling measures, such as financing, continuity can be guaranteed and the quality of care improved. The criteria used for designating centres include transfer of knowledge and willingness to be tested (by visitation). The coordination meeting sees an opportunity to use policy regarding the designation of expertise centres for further knowledge dissemination and organisation of care in the various aspects of the lives of people with rare diseases. The expertise centres must play a central role in this ('spider in the web'). Health insurers have a role when it comes to purchasing care in expertise centres and the surrounding network. IGZ will monitor quality and safety. The Netherlands Healthcare Institute has several roles. It advises the Ministry of Health, Welfare and Sport on the inclusion of orphan drugs in the package and can also stimulate the development of care standards for rare diseases, which often originate from scientific associations. Perseverance may also be needed here if no progress is made. The coordination consultation advocates a sustainable government policy. This policy should focus on three aspects: 1. Further development of new criteria for designated centres with regard to networking and collaboration in the network and collaboration with people with rare diseases and their organisations. Solid support, such as financing, is a requirement for this. 2. Monitoring and evaluation of expertise centres with the possible consequence that centres that do not meet the criteria are closed down or merged (concentration) 3. Designation of new centres of expertise. In addition to the criteria used to designate the expertise centres, the ability of expertise centres to a) build and maintain networks must also be assessed; b) to give practical shape to the connection between the medical and social domains in the network; and c) actively involve organisations of people with a rare disease. **Specific recommendations:** Develop sustainable policy with regard to expanding the tasks of expertise centres and setting up their networks between centres and care surrounding the patient group (in the patient's region). The centres function as a 'spider in the web'. ▪ Set up a monitor for the coming years to monitor the progress of centres and their activities network, for example by a committee. The experiences of Orphanet and VSOP and NFU13 can be used for this. ▪ Set up an external assessment framework (accreditation). When assessing progress and testing, the target group, people with a rare disease, should be given an important voice and facilitated. **Preconditions must be included in policy measures that encourage the formation of a knowledge, care and treatment network and, in the long term, make it mandatory via assessment criteria:** ▪ make available through a program subsidy for research that is in line with the group of diseases that fall under the centres and that are in line with patients' priorities. Not only medical research, but also quality-of-life research, organisation of care research or (care) outcomes research. National and international (European) ▪ measures for the prescription of orphan drugs by the expertise centres or to them affiliated practitioners ▪ measures for reimbursement of orphan drugs through these centres and monitoring operation of orphan drugs

	▪ measures that remove barriers to cooperation between specialists and the different echelons, especially with regard to financing chain care and shared care; - reimbursing/subsidizing the setting up of a network structure ▪ setting up national uniform coding and registration for all expertise centres and their networking ▪ facilitating measures (training, financing) for the participation of patients (organisations) ▪ There is also an important role for health insurers to finance this care and ensure continuity, such as financing network care and expertise centres within expertise networks. Innovative ways (of financing) are needed to organize care for patients with a rare disease. **<u>Coordination, networking</u>** Coordinating care and forming networks is a task that mainly lies with the expertise centres themselves. If necessary, the government can create a number of preconditions for this or remove obstacles. The expertise centres must fulfil a primary role in collaboration with patients, because they have the expertise (and collect new knowledge) about the (group of) rare diseases for which they are designated. Patients and their families prioritized coordination of care as one of the most important action points in the 2013 update of the National rare diseases strategy. *Coordination of care* There is a need for a point of contact/coordinator for coordinating care/assistance for the patient and his/her family. The expertise centres still need to take a big step in this regard. This requires customisation per target group. For some conditions, people often come to a centre and there is sometimes a waiting list. Patients rarely come to the centre for other conditions. The networking around the expertise centre plays an important role in this. In many cases, care and assistance is (also) provided close to home (for example at the GP). EHealth offers options for relocating (part of) care to the region (consultation). This is sometimes described as: 'the knowledge travels, not the patient'. The quality standard must be leading within the network. However, a standard has currently only been developed for a limited number of conditions. **Bottlenecks in the rare diseases strategy:** ▪ Many recognized expertise centres do not yet have a central contact person or coordinator designated (for example, doctor in charge, coordinating nurse, case manager, care coordinator). Moreover, the tasks and responsibilities in centres where there is a coordinator are different. These contact persons/coordinators can also play an important role in forming and maintaining networks. ▪ The current financing system (such as DBC) has a number of obstacles to providing multidisciplinary care (from different healthcare institutions and various laws) to a patient. There is a need for a budget and coordinator that transcends echelon. There is no clear policy regarding the financing of shared care. ▪ The transfer of care for children to care for adults is still insufficient **Specific recommendations:** ▪ Expertise centres (national) must share their experience about the organisation of care and therapy. Expertise centres can learn from other networks for chronic conditions, for example ParkinsonNet or oncology networks. ▪ There are still many rare diseases for which there is no expertise centre (designated). Encourage the formation of expertise centres also for these undiagnosed patients. In the case of very rare conditions, encourage connections to existing centres with expertise in similar conditions in the Netherlands or abroad (ERN) ▪ Expertise centres could make use of collaboration agreements/covenants that already exist for more common conditions or of rare disease networks that have already drawn up this.

	▪ Expertise centres serve within the network of child and adult care and transition from child to child organize adult care ▪ Expertise centres should invest in knowledge sharing, using ICT and EHealth, Shared Care models. **<u>Improving the quality of care</u>** Quality of care for rare diseases must be recorded in a multi-year plan of an expertise centre, which is coordinated with the board of directors and patient organisations. This plan should form the basis for progress discussions and assessment. Improving the quality of care should be interpreted broadly and lead to an improvement in the quality of life. The care surrounding the patient often takes place close to home, in coordination with an expertise centre. An expertise centre provides highly specialized complex patient care from a multidisciplinary team, especially in the areas of: - diagnostics - care, treatment and collecting and sharing new knowledge (research, training). **Diagnostics** **Bottlenecks:** ▪ There is still insufficient recognition (correct/incorrect) of (hereditary) rare diseases among doctors, both in the 0th line (for example the youth doctor), 1st line (for example the general practitioner) and 2nd line (specialists in regional hospitals). Often complaints are not recognized as consistent with a possible rare disease that requires referral. ▪ Preconception care is currently offered to a limited extent in the Netherlands. Although there is one NHG standard preconception care, there is still a lot of unfamiliarity among care providers. Carrier testing is offered in various places, but these options are rarely used. **Specific recommendations:** ▪ Recognition of (hereditary) rare diseases is not sufficiently guaranteed in basic medical training (framework plan) and in the training requirements of general practitioners and paediatricians. NFU and professional groups have a role to play in improving this. ▪ Expertise centres and their networks must be easy to find, especially for referrers (in regional hospitals). The Clinical Genetic Centres also play an important role here when it comes to hereditary or congenital rare diseases. **(After) Care, support and treatment** **Bottlenecks:** ▪ The patient perspective does not yet have a structural place in the various aspects of care, treatment and research. Experiential knowledge must be given a place and be connected to professional knowledge. ▪ The government's focus is often on the high costs of treatment with an orphan drug. However, it not only costs money, it also provides people with quality of life. Moreover, Dutch fundamental and translational medical research makes an important contribution to the development of orphan drugs. There is discussion about the price of this group of medicines. ▪ The ministry has already focused on price negotiations with pharmaceutical companies and cooperation on this with other in Europe. ▪ There is still too little collaboration with patients in the development of medicines. As a result, there is often a lack of relevant outcome measures regarding the improvement of quality of life. Too few innovative ways are being investigated to measure these outcomes. Expertise centres could play a central role in (coordination of) research into new treatment methods and the development of (orphan) medicines and relevant outcome measures. ▪ The structured collection of high-quality data that is suitable for determining variation, natural history and treatment effects is not yet sufficiently guaranteed. Independent registers must be part of expertise centres. ▪ Setting priorities for research is not yet done sufficiently with the target group patients.

	▪ There is not yet a quality standard or treatment guideline for many rare diseases. Often no money and manpower has been made available for this within the scientific association due to prioritisation for common disorders. Cooperation from professional groups and health insurers is necessary, but this does not yet happen in practice. **Specific recommendations:** ▪ Include the patient perspective and experiential knowledge of people with rare diseases decision-making and in medical and social scientific research. Such as determining priorities, data on natural history, relevant outcome measures, start and stop criteria, aspects of quality of life. ▪ Gather new knowledge about the impact of a rare disease, new diagnostic methods, new treatment options, psychosocial guidance, or options for prevention. And think about good distribution in the network and beyond. ▪ Create a uniform national basic registration of people with a rare disease, preferably linked to DHD. Examples of this can be found in muscle diseases and adrenal gland disorders. Ensure sustainable financing of high-quality and independent registers (with research data, for example on the effectiveness of treatment) linked to expertise centres. ▪ The composition and knowledge level of the teams in the expertise centres must match what is needed and what is described in the guideline and quality standards. Also consider disciplines such as doctor for the mentally handicapped, psychologist and social work, WMO consultants or medical examiner. ▪ The best care and treatment should be recorded in new or updated ones standards and guidelines. Scientific associations must organize manpower and financing to develop and keep quality standards and guidelines up to date. Starting with the rare diseases for which centres have been designated. The development of standards for these rare diseases could be included as an extra incentive on the multi-year agenda of the Healthcare Institute. Very rare diseases can be connected to generic modules for (rare) diseases for which a standard has already been developed. International standards can be adopted/reused, also using the networks in Europe (ERN). ▪ Health insurers also have a role here, with regard to purchasing sustainable care and making use of the recognized centres and their network.
Governance and organisational structures	All recommendations in the national rare disease strategy are owned by the listed parties. The national policy regarding the powers and responsibilities of expertise centres lies primarily with the Ministry of Health, Welfare and Sport. Health insurers have a role when it comes to purchasing care in expertise centres and the surrounding network. IGZ will monitor quality and safety. The Netherlands Healthcare Institute has several roles. It advises the Ministry of Health, Welfare and Sport on the inclusion of orphan drugs in the package and can also stimulate the development of care standards for rare diseases, which often originate from scientific associations.
Funding model	Health insurers have a role when it comes to purchasing care in expertise centres and the surrounding network. The document also mentions throughout that funding is required but does not specify where from. Funding issues related to: ▪ measures for reimbursement of orphan drugs ▪ measures that remove barriers to cooperation between specialists and the different echelons, especially with regard to financing chain care and shared care; - reimbursing/subsidizing the setting up of a network structure ▪ facilitating measures (training, financing) for the participation of patients (organisations) ▪ health insurers to finance this care and ensure continuity, such as financing network care and expertise centres within expertise networks. Innovative ways (of financing) are needed to organize care for patients with a rare disease.

References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	*Mentioned in Results (in 2014 – 2016) from the National Rare Diseases Plan 2013 (see additional information).*
Personalised medicine, genomics, genetic counselling	*Clinical Genetic Centres are recommended within Diagnostics.*
Models of care/care pathways	*See "Improving the quality of care" in Implementation actions.*
Workforce	Training opportunities are mentioned in Results (in 2014 – 2016) from the National Rare Diseases Plan 2013 (see additional information) – section "Familiarity with rare diseases". Additionally within Improving the quality of care, a recommendation is - Recognition of (hereditary) rare diseases is not sufficiently guaranteed in basic medical training (framework plan) and in the training requirements of general practitioners and paediatricians. NFU and professional groups have a role to play in improving this.
European Reference Networks	In recommendations from the coordination meeting - care networks with expertise centres (also think of European reference networks) as a 'spin in the game' web' with specific attention to the (psycho)social domain. Additionally, as a result of the National Rare Disease Strategy designation of 300 Dutch expertise centres and 24 European Reference Networks (ERN), five of which are coordinated from the Netherlands.
EU alignment and participation	Mentioned as a recommendation within Direction and Continuity, role for the government – make available through a program subsidy for research that is in line with the group of diseases that fall under the centres and that are in line with patients' priorities. Not only medical research, but also quality-of-life research, organisation of care research or (care) outcomes research. National and international (European). Mentioned as a bottleneck in (after) care, support and treatment - There is discussion about the price of this group of medicines. The ministry has already focused on price negotiations with pharmaceutical companies and cooperation on this with other countries in Europe. Also as a recommendation International standards can be adopted/reused, also using the networks in Europe (ERN).
Health information (including rare disease registries)	Mentioned as a recommendation – uniform coding, national registration of core patient data; serves for this purpose funding and a bottleneck - The structured collection of high-quality data that is suitable for determining variation, natural history and treatment effects is not yet sufficiently guaranteed. Independent registers must be part of expertise centres. Further recommendation in Diagnostics - Create a uniform national basic registration of people with a rare disease, preferably linked to DHD. Examples of this can be found in muscle diseases and adrenal gland disorders. Ensure sustainable financing of high-quality and independent registers (with research data, for example on the effectiveness of treatment) linked to expertise centres.

	Recommendations - infrastructure for collecting and sharing knowledge, sustainable use of eHealth and ICT options in healthcare and expertise centres should invest in knowledge sharing, using ICT and EHealth, Shared Care models.
Orphan medicines	Mentioned in regards to: ▪ financing and reimbursement ▪ measures for the prescription of orphan drugs by the expertise centres or to them affiliated practitioners
Rare disease research	Mentioned throughout. Specific instances include: ▪ the most important recommendation of the coordination consultation concerns the development of policy with which care (coordination), knowledge transfer and research are concentrated in these recognized expertise centres and can be expanded through their network for the benefit of people with rare diseases ▪ financing long-term research programs for rare diseases, both nationally and internationally, aimed at pathogenesis and (psychosocial) treatment ▪ results from the rare disease strategy (see additional information) ▪ make available through a program subsidy for research that is in line with the group of diseases that fall under the centres and that are in line with patients' priorities. Not only medical research, but also quality-of-life research, organisation of care research or (care) outcomes research. National and international (European); ▪ include the patient perspective and experiential knowledge of people with rare diseases decision-making and in medical and social scientific research. Such as determining priorities, data on natural history, relevant outcome measures, start and stop criteria, aspects of quality of life.
Alignment beyond the healthcare sector	*See Theme or Priority Medical and Social Domain.*
Any additional information (for example, background to the strategy or strategy development)	The coordination consultation is composed of the parties that represent the field broadly and have been identified as 'problem owners' in the recommendations in the NPZZ 2013. In addition, the coordination consultation has been advised by patients through grassroots consultations with VSOP and Ieder(in). (Ieder(in) = the Dutch umbrella organisation for people with disabilities and chronic diseases). **<u>Results (in 2014 – 2016) from the National Rare Diseases Plan 2013</u>** After 2013, various parties started activities related to the recommendations from the NPZZ. For example, the NFU, Orphanet and VSOP have been actively involved in the designation of expertise centres. The Health Insurers Innovation Fund has invested 2.8 million euros in a number of implementation projects specifically in the field of rare diseases. *Centre of Expertise* The designation of 300 Dutch expertise centres and 24 European Reference Networks (ERN), five of which are coordinated from the Netherlands, is an important step forward. Criteria derived from the recommendations of the NPZZ and EUROPLAN (European criteria) were used for the designation of the Dutch expertise centres. The assessment criteria for recognizing current expertise centres mainly relate to the presence of multidisciplinary care, leading scientific research and support from the Board of Directors of the healthcare institution to

	which the expertise centre belongs. The NFU, the supporters of the VSOP and Orphanet played an important facilitating role in the assessment process. Erfocentrum, together with Orphanet, ensures the findability of the recognized expertise centres on their websites. *Diagnostics* On the advice of the Health Council, heel prick screening will be expanded in phases to include 14 conditions in the coming years. This improves diagnostics for a large group of rare diseases that can be diagnosed at birth, allowing timely treatment to be initiated to prevent or limit health damage. The Biotechnology and Genetics Forum (FBG) advised the minister in its report on June 14, 2016. 'Early detection of rare diseases', with a proposal for additional screening at the ages of 1 and 10 years. The minister's wish to conduct research into screening for conditions that are not (yet) treatable has been incorporated into this. A response from the minister to the FBG description will follow. The improvement of genetic diagnostics is receiving a lot of attention within the discipline of genetics. The capacity with regard to the above-mentioned heel prick still deserves attention from paediatricians and clinical genetic centres. New (genetic) diagnostic techniques can enable rare diseases to be identified earlier. This also results in new diseases being discovered in people who previously remained undiagnosed. A number of projects are underway in the field of Personalized Medicine, in particular diagnostics of rare diseases. A project has been started on early detection, financed by the Health Insurers Innovation Fund. A diagnosis is not yet possible for a large group of patients with a rare disease. The VSOP has a ZON platform for this group with associated website. *New legislation* There is new legislation that is important for people with rare diseases. The decentralisation legislation (WMO 2015, Participation Act and Youth Act) plus the WLZ and the Appropriate Education Act also have consequences for the care and support of people with a rare disease. One of the most important changes is that municipalities are now responsible for a large part of the policy that is relevant for people with a rare disease. But partnerships between schools, healthcare institutions, housing associations, transport companies, the UWV and employers also determine the possibilities for social participation of this group. People with a rare disease often have a disability or (work) limitation, and the Participation Act is important to them, as is the UN Handicap Convention. The Ministry of Health, Welfare and Sport has been designated as a focal point and as such is responsible for coordinating the implementation of the UN treaty in Dutch legislation and policy. For care across borders, the law on cross-border care offers the opportunity to request expertise outside national borders if it is not available in the Netherlands. Patients also expect that European Reference Centres (ERNs) can contribute to access to expertise elsewhere. The law regarding research on minors is important for research.8. After all, the majority of rare diseases manifest themselves in childhood. This change in the law allows children to be better involved in research. *Familiarity with rare diseases* In the NPZZ, the importance of awareness of rare diseases is mainly linked to early recognition of rare diseases and the role of youth and general practitioners in particular. Various activities have been developed in this regard. For example, the Erfocentrum, together with VSOP, the Dutch Association for Paediatrics (NVK), the Dutch Society of General Practitioners (NHG) and Youth Doctors Netherlands (AJN), has started developing three further training courses (E-learning). In November 2016, the NHG held a successful and well-attended general practitioner conference aimed at paying attention to the early detection of rare diseases. In 2017, an NFU committee will start working on the new framework plan for the Medicine course, for which the coordination consultation will provide input. *Information provision*

	Great progress has been made in the field of information provision. In addition to various associations of people with rare diseases, VSOP and Erfocentrum have invested in various new websites and new content. *Voice of people with a rare disease* VSOP, Ieder(in) and the Patient Federation of the Netherlands have sought cooperation to adequately represent the voice of people with a rare disease, both in the field of cure and care. Through both VSOP and Ieder(in), people with rare diseases can provide input for policy via a platform. Input for this final advice was also provided via these organisations. *Orphan drugs* The Dutch Healthcare Institute published a report in November 2015 published on package management of orphan drugs. VWS collaborates in the field of price negotiation of orphan drugs. *Research* Until April 2016, ZonMw has participated in four E-Rare JTC and has funded a total of 42 Dutch research groups in 32 projects. A number of projects are still ongoing from PM Rare and E Rare. However, there is no budget specifically for rare disease research, not even for new rounds in E Rare. Dutch research is leading. In any case, this appears to be the case for neurological disorders and metabolic disorders. The Dutch output of medical research is above average compared to the Dutch contribution to other medical research for more common conditions.9 Moreover, researchers in the Netherlands focuses on rare diseases that receive relatively little attention elsewhere. This suggests that Dutch researchers act as pioneers in less researched rare disease areas. For Dutch researchers who are active in a specific disease area (with an orphan drug), this results in above-average knowledge production and more often associated with entrepreneurship. (Medical) expertise outside the centres. The strong knowledge production position of the Netherlands and its interactions with entrepreneurial activities suggest that there are a number of current 'innovation hubs' for rare diseases in the Netherlands. The research and publications mainly come from the recognized expertise centres and their research network. The largest share of funding for this medical research is provided by ZonMw/NWO. However, there is currently no clarity about follow-up financing. On February 28, 2017, research into rare diseases will be put on the agenda on Rare Diseases Day 10 and a (draft) agenda will be drawn up from different perspectives (patients, practitioners, researchers, pharmaceutical companies, insurers, etc.). A research agenda will be offered as an addendum to the final advice to the Ministry of Health, Welfare and Sport.

Key: IGZ: Dutch Health Care Inspectorate; GP: General Practitioner; DBC: Diagnose Behandeling Combinatie (Diagnosis Treatment Combination); ERN: European Reference Network; DHD: Dutch Hospital Data; EUROPLAN: European project on National Plans for rare diseases; NFU: Dutch Federation of University Medical Centres; VSOP: Association of Collaborating Parent and Patient Organisations for rare and genetic disorders; UN: United Nations; E-Rare: European cooperation in the field of rare disease research; JTC: Joint Transnational Call; NWO: The Dutch Research Council.

Note: The information in this table was extracted from a version of the original document translated to English using Google Translate.

Table B19. Data extracted for Northern Ireland (Action Plan)

Northern Ireland	Strategy information
Author(s) **Title**	Northern Ireland Department of Health Northern Ireland Rare Diseases Action Plan 2022/23[34]
Timeline	April 2022 to March 2023 Once published, action plans will be updated and reviewed annually to measure progress, update actions, or add new ones.
Overall aim(s)	Through this action plan, we will take the first steps in Northern Ireland towards achieving our overarching vision – delivering improvements in diagnosis, awareness, treatment and care, and creating lasting positive change for those living with rare diseases.
Themes and or priorities	*Note: Priorities and Themes as per UK Rare Diseases Framework* **Priorities** 1. Helping patients get a final diagnosis faster 2. Increasing awareness of rare diseases among healthcare professionals 3. Better coordination of care 4. Improving access to specialist care, treatment and drugs. **Underpinning Themes** ▪ Patient Voice ▪ National and international collaboration ▪ Pioneering research ▪ Digital, data and technology ▪ Wider policy alignment.
Targets (if specified) and measurement method(s) (where available)	*See 'Key milestones and measures (Year 1)' listed under each action.*
Implementation action(s), lead(s) and key performance indicator(s)	**Priority 1: Helping patients get a final diagnosis faster** **1. Information Hub** An online Rare Disease Information Hub established for NI, with a dedicated person employed to: ▪ collate relevant information; ▪ act as a contact point and source of advice for people living with a RD in NI and their families; ▪ connect those working in the RD field. *Key milestones and measures (Year 1):* ▪ Scoping Group established. ▪ Scoping review with recommendations for a best practice model. ▪ Identification of resources/budgets required. ▪ Secure funding for a dedicated person/s (to include RD navigators) to take the Hub work forward through relevant business case or funding application to appropriate funding organisation.

	Related Year 1 Action Plan actions: 7. Expert centre; 9. Mental health needs; 10. Patient portal. **2. Agree a new NI Genomics Partnership model to deliver against the UK Genome Strategy** Genomics Medicine Service established in NI, working with delivery partners across government, Health and Social Care (HSC), academia, industry, patients, and Republic of Ireland (ROI) counterparts, to agree future vision and policy decisions on genomics development and provision in NI, linking and collaborating with the UK nations in line with the commitments of *Genome UK: The Future of Healthcare*, the national strategy for genomic healthcare. *Key milestones and measures (Year 1):* ▪ Develop governance structure for Regional Genomics Medicine Service, in partnership with key delivery partners, including links with ROI. ▪ Genomics working group agree governance structure and accountability. ▪ Ministerial approval to commence with new Service; ▪ By end of year one, to have held the first meeting of the new NI Genomics Medicine Partnership. *Related Year 1 Action Plan actions:* 8. Care pathways/models; 11. Improve access to Rare Diseases (RD) drugs; 12. Improved access to other RD specialist teams locally, nationally and internationally. **3. Review newborn screening** Newborn screening to be reviewed in line with the population needs of NI. *Key milestones and measures (Year 1):* ▪ Participate in UK National Screening Committee (NSC) - follow guidance to ensure appropriate use of genetics in line with NSC recommendations. ▪ Establish Task & Finish Group (including patient voice) to scope newborn screening needs for NI, taking geographical prevalence of conditions on an all-Island basis into account. ▪ Produce a scoping review to include recommendations for optimised screening for conditions in NI. ▪ Ensure NI representation in all new UK screening initiatives. *Related Year 1 Action Plan actions:* None. **Priority 2: Increasing awareness of rare diseases among healthcare professionals** **4. Develop a Northern Ireland Rare Diseases Registry** A NI Rare Disease and Congenital Abnormality Registry (NIRADCAR) to be established and linked to the new Encompass Integrated Care Record. *Key milestones and measures (Year 1):* ▪ Quarterly devolved nations meetings with registry colleagues to work towards a UK-wide national rare disease registration facility. ▪ Registry Lead appointed and Registry Steering Group established. ▪ Identify how best to obtain a minimum core dataset and standardised coding for the registry. ▪ Develop inclusion criteria and analysis plans, taking account of stakeholder input from all relevant sectors, ensuring individual condition registry specialists are included. ▪ Scope logistics for accommodating the NI rare disease registry ▪ Work with the NI cancer registry to generate the first factsheet for rare cancers in NI. ▪ Source registry information for 1-2 individual RD conditions associated with exemplar care pathways. ▪ Scoping review completed and business case developed to include necessary resources to take registry work forward.

Related Year 1 Action Plan actions: 1. Information Hub; 7. Expert Centre; 8. Care pathways/models; 9. Mental health needs; 10. Patient portal; 13. RD research awareness/participation.

5. Education & Training - pre & post registration. Education co-ordinator

Build on links with external organisations providing training.

Key milestones and measures (Year 1):

- Education & Training Steering Group established to include relevant stakeholders, with emphasis on patient and public involvement/Co-production, design, and delivery.
- Secure funding for a dedicated person to take the E&T work forward.
- Cost / benefit analysis completed to support a bid for additional resources.
- Ensure continuing professional development (CPD) accreditation for postgraduate training events.
- Representatives to promote/disseminate CPD event. Information through websites and social media channels.
- Build on existing RD awareness sessions and deliver 12 sessions per year in partnership with relevant bodies.
- Embed delivery of RD teaching sessions, including the patient voice, to all healthcare professionals, including undergraduate medical, biomedical, nursing and Allied Health Professional students, as well as postgraduate taught students.

Related Year 1 Action Plan actions: 1. Information Hub; 4. Registry; 6. Increase awareness across communities; 7. Expert Centre; 8. Care pathways/models; 9. Mental health; 10. Patient portal; 11. Improve access to RD drugs; 12. Improved access to other RD specialist teams; 13. RD research awareness/participation.

6. Raise awareness of rare diseases across a range of communities

Increase the profile and public awareness of rare diseases through public events such as Rare Disease Day, RD Campaigns, and establishment of an All-Party Group on Rare Disease.

Key milestones and measures (Year 1):

- NIRDP support to the All-Party Group for RD.
- Host Annual All-Ireland Rare Diseases Day Conference.
- Host at least 2 rare disease focused Science, Technology, Engineering and Maths (STEM) initiatives in 2022.
- Promotion/ dissemination of information on events through websites and social media channels.
- Bi-monthly All-Ireland RD webinars through All Ireland Students for RD network.
- Quarterly RD discovery research meetings planned with both professional/public components.
- Deliver 12 webinars, information sessions or campaigns to raise awareness amongst the wider community.
- Implement training initiatives to empower patient group representatives to be active voices for their own groups and broader RD community in all rare areas, but particularly for more complex areas, for example, research and development.

Related Year 1 Action Plan actions: 5. Education & Training; Other Actions links as per Action 4.

Priority 3: Better co-ordination of care

7. Develop an expert centre for Rare Diseases to include RD specialisms co-ordinator

Develop a national rare disease care centre acting as a central point of contact for rare disease across NI.

Appoint a rare disease specialists information co-ordinator.

Key milestones and measures (Year 1):

- Scoping group captures the NI landscape plus further afield and develop an options appraisal.

	▪Determine requirement for physical space – consider hybrid model. ▪Develop a Business Case/implementation plan for developing an expert centre and specialism coordinator. *Related Year 1 Action Plan actions:* 1.Information hub; 2. Genomics; 3. Registry; 8. Care pathways/models; 9. Mental health needs; 10. Patient portal. **8. Develop care pathways/models of care.** Access to services in the UK & elsewhere. Define "what a better care model looks like". More patient information on all available services, including transition from paediatric to adult care. Clear patient information to enable understanding for example, infographics & lay terms/non-medical terminology. *Key milestones and measures (Year 1):* Establish a working group to: ▪Develop a pathway for individuals with suspected, but not yet diagnosed RDs, for example through regular gene discovery clinics. ▪Develop a methodology to deliver exemplar care pathways for 1-2 individual RD conditions in the first year with a view to use as a template for other RD conditions. ▪Engage with/ recruit RD clinicians to participate in the 'clinician builder programme' to develop skills for clinical input to the building of RD pathways, including 'red flag' signposting and other needs. ▪Recruit and work with Paediatric, Adult RD Clinical Leads as well as other individual clinical leads to push forward work on agreed pathways/ defined service specifications. ▪Continue to improve a virtual & face to face mixed model for consultations to connect patients with the clinicians they need. ▪Scope existing individual RD voluntary organisation work in this area to determine best practice examples. *Related Year 1 Action Plan actions:* Action 8 is important to all other Actions and collaboration is required with all working groups, depending on the individual item under consideration. **9. Ensure the mental health needs of rare disease patients and carers are included across all appropriate NI Government strategies and programmes.** This includes provision of support in areas wider than the health service, for example social care, housing and education. Within Mental Health services, to focus on enhancing wellbeing and providing counselling support for people with rare diseases. To consider Child and Adolescent Mental Health Services being open to patients through the hub. Clinicians enabled to refer directly into Mental Health services. *Key milestones and measures (Year 1):* ▪Largely included in the Information Hub, the Expert Centre and developing pathways and models of care, and should be embedded in those actions. However, given the importance of mental health for RD and Action 22 of the MH Strategy, this will remain as a standalone Action to ensure it is appropriately addressed. ▪This may include scoping appropriate links through other Actions to ensure that clear pathways are identified between all relevant support organisations. ▪Identify what support functions already exist within healthcare provision and the community & voluntary sector, and determine where gaps exist (gap analysis). *Related Year 1 Action Plan actions:* 1.Information hub; 2.Registry; 5. Education & Training; 7. Expert centre; 8. Pathways/models; 14. RD Champion.

	10. Patient portal A "one stop shop" where a patient can view information, with access to all communications, healthcare professionals, summary care record and emergency care record. *Key milestones and measures (Year 1):* ▪Work / liaise with relevant people in working groups across other Actions to ensure input is provided. ▪UK RD Framework is considered by the NI Digital Strategy (encompass) team during the design, build and rollout of the programme. ▪Liaise with encompass to familiarise potential users (clinicians and patients) with the functionality of MyChart. ▪Ensure appropriate information (leaflets/online instruction) is available for RD patients. ▪encompass team to carry out a RD specific public engagement event to provide an update on the current position of encompass and how it may benefit the RD community in terms of a patient portal. *Related Year 1 Action Plan actions:* 1. Information hub; 4. Registry; 7. Expert centre. **Priority 4: Improving access to specialist care, treatments, and drugs** **11. Improve access to Rare Disease drugs** Ensure equity of access to RD medicines locally, regionally, and nationally by increasing health professional and patient awareness of the existing mechanisms to access available initiatives. *Key milestones and measures (Year 1):* ▪Ensure appropriate RD representation and contribution (including patient voice) during the development of policy processes around access to, and managed entry of medicines, including the Individual Funding Request mechanism, into the NI healthcare system. ▪Working with delivery partners, produce information resources and a clear roadmap for available initiatives. ▪Explore options for hosting all information digitally in one locality. ▪Over the coming year, work will be undertaken to review the Managed Entry of New Medicines process and augmenting current processes such as access to innovative medicines and participation in wider procurement opportunities. *Related Year 1 Action Plan actions:* 7. Expert centre; 8. Care pathways/models; 10. Patient portal. **12. Improve access for clinicians and patients to other rare disease specialist teams – locally, nationally, and internationally** Improve awareness of available processes for access to local, national, and international specialist teams. Provide support for local health professionals and patients to access tertiary specialist centres where local specialists are unavailable. Develop clear mechanisms and/or increase awareness of existing referral mechanisms for UK, all island and wider/international. *Key milestones and measures (Year 1):* ▪Explore digital hosting options for all information. ▪Ensure all relevant options are clearly detailed and accessible online by end of year. ▪Provide clear instruction on pathway to tertiary specialist centres. *Related Year 1 Action Plan actions:* 1. Information hub; 7. Expert centre; 8. Care pathways/models; 10. Patient portal. **13. Improve awareness of and participation in rare disease research** Increase health professional awareness of NI Clinical Trials Network and other UK clinical trial databases. Encourage uptake of suitable / available clinical trials amongst healthcare professionals. Create transparency for patients around the mechanisms and entry opportunities for clinical trials. Advise suitable NI patients about current clinical trials in NI.

	Key milestones and measures (Year 1): Establish a short working group to refine and review the following tasks by the end of the year: ▪Establish a baseline of current rare disease studies recruiting NI patients. ▪Review participation of NI patients in clinical trials/research elsewhere and understand the models for participation. ▪Regularly review clinical trials and research databases for opportunities to participate. ▪Develop a communication plan to disseminate information on opportunities to participate. ▪Where possible, work with other UK nations to scope and map information and data related to rare disease clinical trials and research studies. *Related Year 1 Action Plan actions:* 1. Information hub; 7. Expert centre; 8. Care pathways/models; 10. Patient portal. **14. Champion for Rare Diseases in NI** *Key milestones and measures (Year 1):* ▪ Scoping exercise to explore/ consider role and requirement for additional resources. Develop outline proposals with an options appraisal. ▪ Consider joint role between statutory/university/voluntary sector reps. *Related Year 1 Action Plan actions:* 5. Education & Training; 6. Increase awareness across communities.
Governance and organisational structures	**UK-wide implementation** The Framework is a UK-wide document. However, each of the four UK nations has its own delivery or implementation group responsible for drafting and monitoring nation-specific action plans. All four nations have committed to publishing their action plans by the end of 2022. To further help with implementation of the Framework, two UK-wide boards have been created: 1. The UK Rare Disease Framework Board, providing high level co-ordination of rare disease policy and action plans across the four UK nations; and, 2. The UK Rare Diseases Forum, providing a platform to engage a wide range of stakeholders in the rare disease community for advice and input. The Forum has two parts: a core membership which meets twice a year, and an online knowledge and collaboration platform for continual engagement with a broad range of stakeholders, both of which feed into the strategic UK Rare Diseases Framework Board. **Northern Ireland Action Plan** The NI Rare Diseases Implementation Group develops, oversees and co-ordinates delivery of NI's Action Plan. It brings together key stakeholders across the healthcare system, including representatives from relevant areas such as commissioning, public health, the rare disease patient voice via the voluntary sector, academia, adult social care, mental health, and genomic medicine. The development of NI's first action plan has been informed by more than 2,000 voices from the rare disease community. Over the course of 2021 and 2022, the Implementation Group met regularly to develop and agree the actions which form the basis of the plan. The Implementation Group has worked in partnership to develop this action plan, bringing together representatives from the rare disease patient and public voice, and the clinical community, including: ▪ Department of Health – Secondary Care, Mental Health, Social Care representatives; ▪ Health and Social Care Board – Specialist Commissioning, Pharmacy, Adult Social Care ▪ Public Health Agency – Research & Development ▪ Health and Social Care Trusts – clinicians (paediatric and adult)

	▪ encompass – Northern Ireland digital integrated care record initiative team ▪ Northern Ireland Rare Disease Partnership – umbrella group representing the rare disease community ▪ Queen's University Belfast – researchers and educators ▪ Ulster University – researchers and educators All of these key stakeholders are committed to working in partnership to co-produce, design and deliver this plan as efficiently and effectively as possible to meet the needs of the rare disease community in Northern Ireland. Following publication of this Action Plan, the Implementation Group will continue to meet to co-ordinate and report on delivery and develop actions for our second action plan in 2023. **Monitoring progress** The 2021 UK Rare Diseases Framework commits to working closely with the rare diseases community to ensure that the Action Plans developed are actionable, measurable, and regularly reviewed. Following publication of this Year 1 Action Plan, which has been co-developed with a diverse range of stakeholders including the NI Rare Diseases Partnership, the Northern Ireland Rare Diseases Implementation Group will continue to meet regularly to report on progress and over the next year will work on proposals for new and/or updated actions. It is important to note that it will take time to make progress across all of the actions in this Year 1 Action Plan; some may be delivered in this first year and others should be considered as longer-term plans that need early work to fulfil the vision. Progression of a number of the actions will require development of business cases or funding applications, all of which will be subject to normal approval processes, available funding and value for money. We will also work closely with the four nation delivery/implementation groups to ensure that outcomes are identified and best practice shared throughout the duration of the plan. Most importantly, we will continue to work with patient organisations and charities already performing valuable work under the four priorities of the Framework, and ensure through ongoing dialogue that people with rare diseases remain at the heart of the decision-making process. *Note: Not directly related to governance of the action plan, but a relevant link to the NI Executive.* **All party working group** The NI Rare Diseases Partnership actively lobbied on behalf of, and with support from, the rare disease community to successfully establish an All-Party Group (APG) for Rare Disease at the NI Executive. The APG group will act as a mechanism to ensure that all future conversations around rare disease support and services have a direct conduit into our parliamentary structure at the highest level, whilst supporting awareness raising at an Executive and regional level.
Funding model	*Note: References to funding included in Actions* **Action 1:** It will also be important to secure funding for a dedicated person/s (to include rare diseases navigators) to take the Information Hub work forward, therefore a relevant business case or funding application will be developed. **Action 2:** We will also work to agree an investment and implementation plan by the end of the first year. **Action 4:** Part of the work in developing a NI registry will be to scope the logistics for accommodating the registry; a scoping review is expected to be completed and a business case developed as part of this Year 1 Action Plan, to include necessary resources to take the registry work forward. **Action 5:** We will develop a cost / benefit analysis to support a bid for additional resources, including a dedicated education co-ordinator to take the education and training work forward. **Action 7:** One of the outcomes will be to explore the requirement for a physical space and developing a business case and implementation plan for an expert centre by the end of year one.

	Action 13: Whilst it is recognised that our healthcare system continues to meet significant resource challenges, opportunities for research training to increase the capability and capacity of our HSC rare disease workforce will be actively identified and disseminated, and support provided in identifying and securing appropriate funding for rare disease research studies.
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	*See Action 3.*
Personalised medicine, genomics, genetic counselling	*See Action 2.* **Progress to date: Genomics** Significant strides have been made in helping patients get a final diagnosis faster, for example the publication of *Genome UK: The Future of Healthcare* established the strategic direction for the future of genomics across the UK. Genome UK provides a 10 year strategy to create the most advanced genomic healthcare system in the world, underpinned by the latest scientific advances to deliver better health outcomes at lower cost. Notable Genomic Medicine Service achievements to date include the success of the 100,000 Genomes Project, the establishment of a Regional Molecular Diagnostic Service (RMDS) for NI and the rapid upturn in pathogen genomic sequencing capability in response to the COVID-19 pandemic. Genomic medicine has greatly improved diagnostics and treatments across many areas of healthcare. Following Genome UK, NI has a shared commitment to ensure equity of service and quality of care for our rare disease population and to further support the public health priorities by continuing to enhance both our pathogen and infectious diseases sequencing capabilities. New computer tools such as the Genomics Open Core Engine for Accelerating Northern Ireland Care are being developed as a result of the 100,000 Genomes Project to help clinicians streamline rare disease testing for their patients. Experiences from participating healthcare professionals are supporting the practical day-to-day development of the genomic medicine service for NI. Views from patients participating in the 100,000 genomes project have informed recruitment, regular engagement, and delivery of results for whole genome sequencing.
Models of care/care pathways	*See Actions 1, 7, 8, 9, 12.*
Workforce	*See Actions 5, 6.* **Progress to date: Training and Education** Over the past decade, rare disease teaching has been embedded into undergraduate medical, biomedical and nursing curricula at Queen's University Belfast (QUB), additionally providing postgraduate training and education in rare diseases for students and healthcare professionals, with many sessions including patients and their families speaking directly with students. Rare disease sessions have been integrated to personalised medicine and nursing modules at Ulster University (UU). The NI Rare Disease Partnership and the two NI universities (QUB and UU) have exchanged teaching material and worked together to set up new rare disease teaching sessions and harmonise existing sessions in different courses and schools. There is an evolving programme of local workforce development, including CPD accredited events, to help health and social care professionals use genomics and bioinformatics effectively. This needs to be strategically enhanced and taken forward consistently across NI and is being further considered within the Year 1 Action Plan.

	To stimulate interest in developing a career in the rare diseases field and attract nurses, medical doctors or researchers for the future, the three delivery partners developed a collaborative STEM project and engaged with 70 NI schools and 600 Key Stage 5 students. Five additional STEM activities focusing on raising awareness of rare diseases were delivered from March 2021 to February 2022. Following publication of their quick reference guide for rare diseases, QUB explored rare disease perceptions among the NI General Practitioner community, and regularly host continuing professional development events for HSC professionals. In addition, the NI Rare Diseases Partnership organised training sessions with the Pharmacy Forum and one with the Royal College of General Practitioners in NI, which was delivered by Medics for Rare Disease, a Genetics Clinician from Belfast HSC Trust and QUB.
European Reference Networks	*Not mentioned.*
EU alignment and participation	*See Action 12- refers to access to international teams for those with rare diseases.* **Progress to date: All-island forum** February 2022 saw a new all-island patient centred North/South Rare Disease Forum which will enable individual rare disease-specific patient groups to come together quarterly to discuss areas of common concern or interest. This Forum will go some way towards unifying the key 'expert by experience' voices around the island and working to support identification of services that can be delivered collaboratively to improve quality of life for those with rare conditions.
Health information (including rare disease registries)	*See Actions 1, 4, 10, 12.* **Progress to date: Registry** The initial scoping review on developing NIRADCAR is being progressed in line with the UK Framework agreement and local funding constraints, with five registry scoping meetings held with diverse stakeholders. Several meetings have engaged with Leads of the National Congenital Anomaly and Rare Disease Register (NCARDRS) England, Congenital Anomaly Register and Information Service Wales, and Congenital Anomaly and Rare Disease Registration and Information System (CARDRISS) Scotland, to share best practice and agree common elements across the UK. Several research projects have been conducted to gather preliminary data towards developing NIRADCAR.
Orphan medicines	*See Action 11.* **Progress to date: Access to drugs** The UK aspires to be a world leader for development, testing, access and uptake of new and innovative treatments and technologies. The National Institute for Health and Care Excellence (NICE) is the independent body responsible for providing evidence-based guidance on whether medicines represent a clinically and cost-effective use of NHS resources, ensuring that NHS funds provide the most health benefit for society. NICE assesses the majority of medicines through its standard technology appraisal (TA) programme, but also operates a separate highly specialised technologies (HST) programme for a small number of medicines for very rare diseases. New commercial flexibilities have resulted in NICE appraising all new medicines. The NI Department of Health has a formal link with NICE where TAs are endorsed for implementation within the NI healthcare system where they are legally and policy applicable. Currently NICE is updating its processes and a number of the changes adopted will support timely patient access to innovative medicines for patients with rare diseases. For example, NICE has introduced a new severity modifier for committees to consider the severity of the disease or condition under consideration when making recommendations. This reflects evidence that society values more highly the health benefits for people with very severe conditions, and committees will be able to give additional weight to the treatment benefits for rare and severe conditions under consideration. Where

	there is uncertain evidence in relation to a medicine, a particular issue for rare diseases where the population is small, NICE will adopt a more accepting, flexible and proportional attitude towards evidence uncertainty within its decision making. In addition, NICE is adopting process changes to help improve participation of patients and clinical experts, and has refined the criteria used for identifying an HST which will provide greater clarity and predictability for stakeholders. Over the next year NICE plans to implement these changes to make its methods and processes fairer, faster and more consistent – supporting timely patient access to new treatments, including those for rare diseases. NICE will also continue to provide support to the life sciences industry, including companies developing therapies for rare diseases.
Rare disease research	*See Action 13.* **Progress to date: Current Context** Similarly, safety considerations, redeployed staff and travel restrictions have caused additional barriers to rare disease research, where cohort sizes are often already small. The Clinical Research Resilience, Recovery and Growth Programme, which has a focus on managing the recovery of non-COVID research in the UK, with each country having its own delivery group/programme, will contribute to the building of NI's non-COVID research activity.
Alignment beyond the healthcare sector	*See Actions 6 and 9.* **Action 6: Raise awareness of rare diseases across a range of communities** The difficulties and problems of the rare disease population are wider than healthcare and reach into other domains such as housing, schooling and transport. With this action we commit to raising the profile of rare diseases by increasing public awareness through public events such as Rare Disease Day and other rare disease campaigns. Our key milestones for year one include providing the NI Rare Diseases Partnership support to the NI Assembly All Party Group for rare diseases and hosting the annual all-Ireland Rare Disease Day Conference on a hybrid basis where possible. We also commit to hosting at least two rare disease focused STEM initiatives this year. Our partner organisations, Queen's University Belfast, Ulster University, the NI Rare Diseases Partnership and other rare disease community and volunteer groups, will promote and disseminate information on relevant events through respective websites and social media channels. In addition, we will participate in bi-monthly all-Ireland rare disease webinars associated with the All Ireland Students for Rare Disease Network, and plan for quarterly rare disease discovery research meetings with both professional and public components. To raise awareness across communities we intend to deliver a range of webinars, information sessions and outreach support meetings. Through training we will empower patient group representatives to be active voices for their own discrete groups as well as the broader rare diseases community, particularly in relation to more complex areas such as research and development. **Action 9: Ensure the mental health needs of the rare diseases population are included across all appropriate Northern Ireland Government strategies and programmes.** This action rightly looks first to our mental health services and the needs of the rare diseases population, with a focus on enhancing wellbeing and providing counselling support. However, it also emphasises the broader need for support across all relevant government departments. This includes, for example, the Department for Communities in relation to employment, housing and other accessibility issues, the Department of Education in relation to the Education Strategy and wellbeing needs of rare disease children with complex needs, and the Department for the Economy in relation to further and higher education, and job skills. **Progress to date: Current Context**

	Progress in developing this action plan has taken place against the backdrop of the current COVID-19 pandemic, which has caused significant disruption to the healthcare service. A focus on COVID-19 has meant that some routine and primary care services have been scaled back, leading to delays or cancellations in diagnostic testing, transfusions, surgeries, scans, and routine appointments – all of which have significantly impacted the rare disease community as well as other patient populations. In the context of rebuilding our healthcare system, the Minister has published a *Strategic Framework for Rebuilding Health and Social Care Services* (June 2020) to guide a regional approach to service rebuilding and transformation which places workforce and technology at the heart of long-term planning across the healthcare service. Whilst ambitious, the NI Rare Diseases Action Plan is also realistic, recognising that it may take time to implement change within the current context.
Any additional information (for example, background to the strategy or strategy development)	*Note: Background information on development of UK Framework and NI Action Plan.* Development of the UK Rare Diseases Framework (henceforth the 'Framework' throughout this document) was based on the outcomes of the 'National Conversation on Rare Diseases', launched in 20191. The Conversation gathered views across the rare disease community on the major challenges faced by people affected by rare conditions across the UK. An impressive 6,293 responses were received, which helped identify four high-level priority areas to bring about real change and forming the basis of the Framework. Northern Ireland's first Rare Diseases Action Plan aims to support implementation of the Framework and is for the initial period from April 2022 to March 2023. It has been developed with stakeholders across the healthcare system, the Northern Ireland Rare Diseases Partnership (NIRDP) representing the rare disease community and rare disease researchers and educators from QUB and UU to bring about specific and measurable improvements for people living with a rare disease. The Northern Ireland (NI) Rare Diseases Implementation Group develops, oversees and co-ordinates delivery of NI's Action Plan. The Implementation Group has worked in partnership to develop this action plan, bringing together representatives from the rare disease patient and public voice, and the clinical community, including: ▪ Department of Health – Secondary Care, Mental Health, Social Care representatives; ▪ Health and Social Care Board – Specialist Commissioning, Pharmacy, Adult Social Care ▪ Public Health Agency – Research & Development ▪ Health and Social Care Trusts – clinicians (paediatric and adult) ▪ encompass – Northern Ireland digital integrated care record initiative team ▪ Northern Ireland Rare Disease Partnership – umbrella group representing the rare disease community ▪ Queen's University Belfast – researchers and educators ▪ Ulster University – researchers and educators **Community engagement** In developing the NI Rare Disease Action Plan, we have placed the needs of those living with rare diseases at the forefront. In September 2021, we held an engagement event to offer an opportunity for people living with a rare disease and those working in the field of rare diseases to engage with the action planning process. Attendees included: ▪ carers and family members; ▪ rare disease charities; ▪ healthcare professionals; ▪ industry partners; and,

	▪ researchers. Anyone living or working in the field of rare diseases were offered the opportunity to feed into the action plan in writing at that stage. In addition, the NI Rare Disease Partnership represents the voice of the rare disease community at every Implementation Group meeting and undertook a final roundtable focus group on the draft action plan in March 2022.

Key: APG: All-Party Group; CARDRISS: Congenital Anomaly and Rare Disease Registration and Information System Scotland; CPD: continuous professional development; GP: General Practitioner; HSC: Health and Social Care; HST: highly specialised technologies; NCARDRS: National Congenital Anomaly and Rare Disease Register; NI: Northern Ireland; NICE: National Institute for Health and Care Excellence; NIRADCAR: NI Rare Disease and Congenital Abnormality Registry; NIRDIG: Northern Ireland Rare Disease Implementation Group; NIRDP: Northern Ireland Rare Diseases Partnership; NSC: National Screening Committee; QUB: Queen's University Belfast; RD: Rare Diseases; RMDS: Regional Molecular Diagnostic Service; ROI: Republic of Ireland; STEM: Science, Technology, Engineering and Maths; TA: technology appraisal; UK: United Kingdom; UU: Ulster University; WG: working group.

Table B20. Data extracted for Northern Ireland (Progress report)

Northern Ireland	Strategy information
Author(s) **Title**	Northern Ireland Rare Disease Implementation Group (NIRDIG) Northern Ireland's Rare Diseases Action Plan: Progress Report Year 1 (March 2022 – March 2023)[33]
Timeline	March 2022 – March 2023
Overall aim(s)	This report details the progress made by the NIRDIG in the first year of the *Rare Diseases Action Plan for Northern Ireland* published in March 2022.
Themes and or priorities	*Note: Priorities and Themes as per United Kingdom (UK) Rare Diseases Framework* **Priorities** 5. Helping patients get a final diagnosis faster 6. Increasing awareness of rare diseases among healthcare professionals 7. Better coordination of care 8. Improving access to specialist care, treatment and drugs. **Underpinning Themes** ▪ Patient Voice ▪ National and international collaboration ▪ Pioneering research ▪ Digital, data and technology ▪ Wider policy alignment.
Targets (if specified) and measurement method(s) (where available)	Not mentioned.
Implementation action(s), lead(s) and key performance indicator(s)	**Progress Summary** **Action 1: Information Hub and Action 7: Expert centre** The focus for Work Group (WG) 1 has involved gathering information on the cost and the requirements to set up and establish an online Rare Diseases Information Hub and Expert Centre. Building on work previously undertaken, the key milestone for this first year was to establish a scoping group to consider the detail. However, once work commenced it became clear that the two actions (1 and 7) overlapped and, therefore, should be progressed together. As a result, early discussions across the UK nations to scope the potential for a common, shared Information Hub, including a Northern Ireland (NI) directory linked to emerging resources such as GeNotes as well as country-specific information, have now taken place. Whilst collaboration with England's Orphanet co-ordinator has facilitated NI updates on the Orphanet website, a regional information co-ordinator for NI will be required to provide and co-ordinate local updates. The expected outputs for Actions 1 and 7 include a review paper with recommendations for a best practice model and identification of the resources required to establish an effective Information Hub/Expert Centre. These are better placed to be expanded following the appointment of the Paediatric and Adult Clinical Leads in January 2023. It will also be important to secure funding for a dedicated person(s) to take the Information Hub work forward. Therefore, a business case or funding application will be developed.

	Action 2: Genomics Action 2 of the NI Rare Diseases Action Plan is to agree a new NI Genomics Partnership model to deliver against the Genome UK Strategy. A key milestone was to develop a governance structure with key delivery partners and to consider opportunities for cross-border collaboration. In March 2022, following four Nation Ministerial endorsement and publication of Genome UK: Shared Commitments, a series of UK-wide commitments to work together to implement and realise the potential of genomic healthcare for the benefit of all patients across the UK, former NI Health Minister Swann announced plans for a Department of Health (DoH)-led Genomics Partnership for NI: Exciting future for genomics in Northern Ireland – Swann | Department of Health (health-ni.gov.uk). This Genomics Partnership would bring together delivery partners from across government, Health and Social Care (HSC), pharmacy, public health, industry, research and academia to deliver an integrated genomics service for NI. The Partnership would set the strategic vision and contribute to the development of a NI Genomics Implementation Plan under the Shared Commitments. Early groundwork to establish this Partnership got underway. DoH officials engaged with key stakeholders including the Pathology Network, Commissioners, PHA, Regional Molecular Diagnostic Service, Universities, as well as colleagues from Scotland and Wales, where similar genomics governance structures are well established, and in the Republic of Ireland, to gain insight from experience and inform plans for NI. A Project Initiation Document was developed and a process to identify key delivery partners was commenced. Funding to appoint a Programme Team with Clinical leadership to support the Partnership, was included in the Department's 3-year budget forecast. However, the ongoing absence of a NI Executive throughout 2022/23 and the consequent delay in an agreed Health budget had a negative impact on the Department's ability to plan strategically and invest as needed. Unfortunately, genomics was one such area that suffered from these budgetary constraints and it has not been possible to progress the work at the pace we had anticipated. In his final week in office, Minister Swann published a Statement of Intent for Genomics in October 2022 reiterating his and the Department's commitment to progressing the Genomics agenda as soon as resources would allow. This statement reinforced the strategic direction for genomics and allows us to continue areas of work in order to move quickly whenever funding becomes available. In the meantime, our partners and stakeholders take forward work through research and interest groups, for example a study of the implementation of whole genome sequencing in NI that was published in June 2022. **Action 3: Extend Newborn Screening** The WG has actively engaged in all new UK-wide screening initiatives, to include exploring NI's participation in the national newborn screening research study which aims to evaluate the benefits and risks of implementing newborn genomic screening to accelerate diagnosis and enable earlier access to treatments for rare genetic conditions. **Action 4: Rare Diseases Registry** Regular meetings with Registry Leads across the UK nations to share best practice and agree common elements across the UK have been ongoing throughout Year 1, including England's National Congenital Anomaly and Rare Disease Register (NCARDRS), Wales' Congenital Anomaly Register and Information Service (CARIS, which also specifically captures rare diseases), and Scotland's Congenital Anomaly and Rare Disease Registration and Information System (CARDRISS). Several research projects have been conducted to gather preliminary data towards developing a NI Rare Diseases Congenital Anomaly Register (NIRADCAR), with independent funding obtained in September 2022 to conduct a review of existing coding infrastructure in NI (overlap with WG1) and ensure that it works seamlessly with registries in other jurisdictions. A review of coding rare cancers was conducted in 2022, resulting in the first publication describing rare cancers based on NI population-based data. Meetings have been held with DHSCNI discussing how best to develop and maintain the registration of rare diseases within NI's digital health and social care

	infrastructure, with exemplar rare disease registries funded as research projects. Further work may be constrained by funding resource issues. **Action 5: Education and Training (Pre & Post Registration)** Working Group 3's focus for Year 1 has been on fostering and building the links already in place with UK and Ireland training organisations to collaborate on healthcare education and training, from undergraduate education through to continuing professional development (CPD). This has included scoping the provision of rare disease teaching across the three NI universities with a view to ensuring appropriate rare disease content in curricula and teaching to relevant professions. There have been discussions with Ulster University's School of Medicine on the possibility of including a Student Selective Component on rare diseases during Year 2 of the medical curriculum to increase awareness and knowledge of rare diseases in undergraduate medical students. In addition, a single document explaining the need to embed rare diseases in the teaching program has been developed for circulation across the universities. WG3 has commenced work on the development of a Database of Teaching Material. The content of this database will be targeted towards specific student groups and will be accessible online. A business case proposal is being developed for a dedicated Rare Diseases Teaching & Education Development Officer for NI to work with universities and schools here to ensure that rare disease is fully embedded within teaching as early as possible. **Action 6: Raising Community Awareness** The Group has been researching and promoting existing rare disease webinars and workshops for research and clinical communities such as the All Ireland Rare Disease Inter-Disciplinary Research Network (RAiN) webinar series and the International Family Nursing Association (IFNA) UK-RoI webinar series (*Mental Health Care for the Rare Disease Community)*, as well as World Birth Defects Day, SSCAN (sub-Saharan African Congenital Anomaly Network), and RELAMC (Latin American Congenital Anomaly Network). A Communication Activity Update spreadsheet has been created and shared with NIRDIG members for further dissemination to their professional colleagues. This provides information about future events related to rare diseases; some of these include CPD-type rewards and all raise awareness, some being disease specific and some based on more general themes, such as the forthcoming 'Paediatric to Adult Transition' workshop (hosted by NICE), a webinar by the National School of Healthcare Science on 'Genomic Testing for Rare Disease', and a BioResource Scientific Conference, hosted by the National Institute for Health and Care Research (NIHR). The WG has spent time during Year 1 connecting with schools and colleges to determine a teaching strategy using rare disease case studies, which will include input from patient groups as well as health professionals. An output of this work included arrangements to hold bi-monthly workshops across schools in NI for the academic year 2023/24. Part of this work involved engaging with the Special Educational Needs Advice Centre (SENAC) who reported that only 10 children with a known diagnosis of a rare disease had been referred. Feedback from parents indicated the lack of awareness of rare diseases among SENAC and other stakeholders, with the result that a new action on how to improve understanding of special needs for children affected by rare diseases among educational professionals, and how to better link parents and these organisations, will be added to the Year 2 Action Plan. ***Engagement*** A new All-Party Group (APG) for Rare Diseases has been established over the last year, with secretariat provided by the NIRDP. The APG provides a much-needed voice at the NI Assembly for the rare diseases population, ensuring wider policy alignment by raising issues affecting the rare diseases community and increasing awareness of rare conditions within the NI Assembly, working together to influence positive change for those affected by rare conditions.

	On Rare Disease Day 28 February 2023, Mark H Durkan MLA Chair of the APG, and Deborah Erskine MLA sponsored a Rare Disease Day Celebration in the Long Gallery, Parliament Buildings, on behalf of the NIRDP and Rare Diseases Ireland (RDI), supported by DoH. The successful event saw approximately 160 people participate in the hybrid in-person and virtual event, with the opportunity to connect with members of the rare disease community, including people living with rare diseases, rare disease advocates, healthcare providers, researchers, and policymakers over a networking lunch. The event closed with the launch and first public viewing of a short film from the NIRDP Rare Stories Project; this project worked over 2022 to capture real life stories of people in the NI rare disease community, supported by '*esc films*' with funding from the Rank Foundation. A key aim of the event was to raise awareness and encourage stakeholder engagement. Resulting from connections made at this event, early cross-border discussions have opened between the two Health Department's officials, with intentions to collaborate on rare disease actions where possible and share information, for example on scope of models of care. **Action 8: Pathways** A sub-group was established to look at the transition journey of a rare disease patient moving from paediatric to adult services within the health service, with a rapid literature review and workshop discussions with academics, HSC professionals, public health specialists and patient representatives. Current excellent and sub-optimal practices were discussed across individual medical specialties including cardiology, genetics, respiratory, neurology, metabolic and nephrology, to identify specific areas that are not common to the general population of patients transitioning from paediatric to adult healthcare services. Expert recommendations were presented to WG2 and agreed. The output paper will be shared with NIRDIG during the summer months for consideration. A review of care pathways across a range of diagnostic pathways was conducted, with a focus on time to diagnosis and access to orphan drugs, with a view to developing exemplar pathways. Specific rare disease pathways included spinal muscular atrophy (newborn screening), TSC (tumour), amyloidosis (biopsy / nuclear medicine), and TP53-related conditions (genetic testing). Following a presentation on hereditary amyloidosis, which has a high relative prevalence in NI, and the issues surrounding diagnosis including the availability of DPD scintigraphy, genetic testing, and cascade testing in family members, an amyloidosis subgroup has been formed. A benchmarking exercise on diagnostic testing is underway with a view to developing a business case for a regional service. **Action 9: Mental Health** Action 9, which seeks to ensure the mental health needs of rare disease patients and carers are included across all appropriate NI government strategies and programmes, is inherent across most other actions. NIRDIG has representation from the Department's Mental Health Unit, which is responsible for taking forward NI's Mental Health Strategy, receiving output papers and providing input as necessary. The Mental Health Strategy is implemented via annual Delivery Plans and work to finalise the 2023/24 Plan is ongoing, subject to additional and sustained funding. Action 22 of the Mental Health Strategy commits to ensuring those with physical health problems leading to mental ill health will be provided with the care and treatment they need. This does not mean the provision of dedicated mental health resources within physical health services, but rather the creation of effective pathways to allow individuals to access specialist support, thereby ensuring that patients get the care and treatment they need, when they need it. Whilst Action 22 has not yet been formally commenced, good progress has been made during 2022/23 across the range of Mental Health Strategy actions which will help to improve access to mental health services for all, including those with physical health conditions such as rare diseases. These actions include: implementation of a Regional Mental Health Service, including commencement of process to appoint a Head of the Regional Mental Health Collaborative Board, and development of a supporting implementation plan; completion of a review of the Mental

	Health workforce to inform a future workforce model for mental health services; development of an Outcomes Framework for Mental Health Services to underpin and drive improvements in service delivery, with implementation aligned to encompass; development of an Early Intervention and Prevention action plan to promote mental health across the whole lifespan; and implementation of the Regional Mental Health Crisis Service. Elsewhere, a presentation on Mental Health has been developed by stakeholders led by the Rare Diseases team at Queen's University, with a review of how mental health impacts people diagnosed with rare disease using data from UK Biobank and more locally in NI. Whilst not specific to mental health per se, but encompassing many of NI's actions including mental health, a rapid literature review of the Needs of informal caregivers of people with a rare disease led to a successful funding bid to develop an Online Rare Disease Carer Support Tool in Northern Ireland (RD-CaST-NI), which has been externally funded until 2025. RD-CaST-NI is an interdisciplinary team which will co-develop and pilot an online resource for carers of people diagnosed with a rare disease or syndrome without a name (SWAN). The intended benefits for carers include increased resilience and improved health and well-being through easier access to information and support. **Action 10: Patient Portal** There has been significant investment in the encompass programme, which will transform how everyone in HSC works to share information and how information will be available to both staff and patients, giving patients and service users the ability to view and update their health information. It will also make it easier for staff to view important information about their patients and service users. The WG has been engaging with DHSCNI and encompass on the delivery of the Patient Portal within the encompass programme, to improve rare disease functionality across medical specialties. This will benefit patients by having all relevant information in one place. Once encompass rollout is underway, a rare diseases specific community engagement event with the encompass team is planned. **Action 11: Access to Drugs and Treatments** This action to improve access to specialist drugs and treatments is likely to remain active for the life of the Action Plan as new and more effective medicines become available. Work to increase health professional and patient awareness of the existing mechanisms to access available initiatives will help to improve NI patient access to rare disease medicines locally, regionally and internationally. This includes exploring options for hosting all information digitally in one locality. A quantitative and qualitative study is underway which aims to explore access to orphan drugs in NI. One of the key deliverables for this group is to design a flow diagram for clinicians to clearly illustrate the routes to access rare disease medicines. For example, NI has a formal link with NICE and, therefore, technical appraisals and clinical guidelines recommended by NICE are available to support prescribing here. Since exiting the EU, some divergence on newly licensed products emerged and were resolved on a case-by-case basis; however, once the Windsor Framework comes into force, these issues will be resolved and NI will revert to a UK-wide licensing system. Other routes to accessing rare disease medicines include the Individual Funding Request (IFR) process, Early Access to Medicines Schemes (EAMS) and the NICE Innovative Medicines Fund (IMF). Officials from the four UK nations attend virtual meetings on Repurposing Medicines. The groundwork to collate the numerous access avenues is underway and the design is being considered. This work will be continued into the Year 2 Action Plan. **Action 12: Improve Access to Rare Disease Specialist Teams** Members of WG2 include NI's Commissioners of health services who regularly attend the Rare Diseases Advisory Group (RDAG), that makes recommendations to NHS England and the devolved administrations on developing and implementing the strategy for rare diseases

	and highly specialised services. These are provided to a smaller number of patients (usually no more than 500 patients per year) and are best delivered nationally through a very small number of centres of excellence. In this way, NI Commissioners keep abreast of the range of highly specialised services and patients in NI can access these services through the Extra Contractual Referral (ECR) process. The ECR process is a unique model of access to air and sea travel, including subsistence and companion costs for patients who need to travel to GB. If the patient is too unwell, or needs to be transferred urgently, we have a dedicated air ambulance supported by clinical cover to critical care levels both to and from GB specialist services. **Action 13: Improve Awareness & Participation Rare Disease Research** A review of the NI research landscape has identified a small, but active, rare diseases research community working across clinical and non-clinical disciplines. Rare diseases research is supported by the HSC R&D Division of the PHA, including Northern Ireland Clinical Research Network (NICRN), the Northern Ireland Cancer Trials Network (NICTN), the Northern Ireland Clinical Trials Unit (NICTU), the Northern Ireland Clinical Research Facility (NICRF), the Clinical Translational Research and Innovation Centre (CTRIC) and the Northern Ireland Centre for Stratified Medicine (NICSM). Additional research takes place through the NI Regional Medical Genetics Service, and many clinicians across various disciplines recruit and / or refer patients to studies elsewhere in the UK. Specific networks and groups are taking forward rare diseases research in NI in collaboration with stakeholders from the rest of the UK, Ireland and beyond. These include the recently launched All-Ireland Rare Disease Interdisciplinary Research Network (RAiN) and the Ulster University Alliance against Rare Diseases, amongst others. WG4 has fostered links with the National Institute for Health and Care Research (NIHR) and the Musketeers Memorandum (MM), and data on recruitment of NI participants to studies via the MM has been collected. The NIHR Specialty Lead for Genetics and the MM has agreed to join a meeting of the WG to further explore current as well as future opportunities. Establishment of the Community for Clinical Academic Research in Rare Diseases will also facilitate further collection of information. Whilst the key objective of WG4 was to review and establish a current baseline for the number of rare disease studies openly recruiting patients in NI, the opportunity to participate in the UK-wide Rare Diseases Research Landscape (RDRL) project, which is funded and led by England, provided a wider remit but ultimately a more rounded view of both NI and the other UK nations that would benefit NI patients. Therefore, the Action will be amended for the 2023/24 Action Plan. It is widely recognised by all four UK nations that the rare disease research landscape is not well characterised and that baseline levels of research activity and patient participation opportunities are not easily captured. There are other challenges specific to each individual nation but, through the RDRL Project, a collaborative UK approach is helping to address these. The initial results show that 103 rare disease studies (excluding a COVID-19 study) were open in NI between 2016 and 2022, recruiting 1,602 participants. Most studies were for respiratory conditions, followed by paediatrics, cancer, haematology and renal medicine. The highest number of patients were recruited to cancer, respiratory, renal and paediatric studies. The WG4 four key tasks were: Establishing Baselines and Needs; Improving Accessibility and Uptake; Enhancing Communication and Awareness; and Improving Future Systems and Initiatives. With help from the NIHR, baseline data for network-adopted studies with sites in NI has been produced. Whilst recognising this is not a complete picture of all research activity, the work represents an initial step in better understanding current activity. Data for studies adopted by NICRN and NICTN are now automatically uploaded to Central Portfolio Management System (CPMS) and included in UK figures. However, much activity sits outside of the NICRN and NICTN, and capture of data outside of these networks represents a significant challenge.

	Therefore a Clinical Academic Research Network for Rare Diseases has been established and will enable a more comprehensive picture of NI research activity to be captured. In addition, information on the challenges around infrastructure, training/competency, protected time and the availability of genetic testing to confirm eligibility for studies can be collated for future consideration. At this point, further analyses have not been feasible, but work will continue to gain a clearer picture of current opportunities for patients with rare diseases across all clinical disciplines, mental health and social care. Case studies of current or planned studies taking place in NI are already providing insights into treatment and management of rare diseases, helping to inform and shape service provision and creating opportunities for our patient population to participate in studies. ***Rare Diseases Patient Survey*** A rare diseases patient survey of people who have experienced research studies or clinical trials is in the final stages of proof-reading and ethics/GDPR approval. The survey will be collated into a report and, through the survey, we will ask for people willing to share their stories for inclusion in the report and other learning materials that will be progressed as part of the communication plan to raise awareness. **Action 14: Rare Disease Champion** A key milestone for this action was to develop an outline proposal which explored the role of a Rare Diseases Champion, including consideration of a joint role between the statutory, university and voluntary sectors, as well as identifying the additional resources that would be required. Year 1 has involved an exploration of the advantages of creating a Rare Diseases Champion to highlight and raise awareness of rare diseases, provide advocacy and act as a central point of contact within NI, nationally and internationally. The WG met and sought advice from other NI Champions to understand the range and the remits of different models, and an outline paper has been developed, highlighting potential options for establishing a Rare Diseases Champion but concluding that a preferred option could not be recommended without contributions from the RD community. While the tasks outlined for Year 1 of this action are complete, the action will be updated and rolled forward to Year 2, to facilitate engagement with the RD community to reach a consensus on which Champion model could deliver the most benefit and value for money. This should help inform a more robust proposal on which a business case for a NI Rare Diseases Champion could be developed, subject to available resources and business priorities. **Next Steps** Some of the Year 1 actions are long term goals that will take time and resources to bring to a satisfactory conclusion. Some actions are dependent on funding, whilst others rely on input and collaboration from busy professionals. The 2022/23 Action Plan will be rolled forward into 2023/24; completed actions will be closed off, new actions added and other actions amended to take account of progress during Year 1, and to continue the momentum working towards longer term outcomes that require sustained focus and effort.
Governance and organisational structures	The Northern Ireland Rare Diseases Implementation Group (NIRDIG) oversees and co-ordinates delivery of NI's Rare Diseases Action Plan. Since its establishment in April 2021, it has worked with stakeholders to develop the NI Rare Diseases Action Plan. The group is chaired by the Department of Health's Chief Scientific Advisor and Director of the Health and Social Care (HSC) Research & Development, Professor Ian Young. The NIRDIG's membership includes key stakeholders from across the Department of Health and HSC, representing areas such as commissioning, public health, the Public Health Agency's R&D Division, adult social care, mental health, clinical input from the regional molecular diagnostic service, as well as the rare disease patient voice via the NI Rare Diseases Partnership (NIRDP) and academia (educators and researchers from Queen's University Belfast and Ulster University).

	In considering how best to take forward the work, NIRDIG grouped the 14 actions thematically, for example actions on information sharing or around education and training, and established five Working Groups to take forward each themed group of actions. The five NIRDIG Working Groups have been firmly established, led by members of NIRDIG with representation from NIRDP, as well as stakeholders from across clinical practice, academia, commissioners, research and policy. Each Working Group agreed a Terms of Reference and work plan for Year 1 and beyond and has been working hard throughout the first year to progress actions despite a lack of dedicated resource and funding. The quality of progress made to date is testament to the commitment and drive of our NIRDIG and Working Group members to deliver for the Rare Disease population in Northern Ireland. **Working Group 1** *Led by:* Professor AJ McKnight (QUB) *Actions:* Information Hub (Action 1), Expert Centre (Action 7) and Patient Portal (Action 10) The actions for this group are centred around information sharing. Membership of Working Group 1 (WG1) includes stakeholders from organisations such as Queens University Belfast, Ulster University, Department of Health (DoH), Belfast HSC Trust and NIRDP. Connecting the necessary stakeholders initially proved challenging; therefore thirteen 'small group' meetings were held between June 2022 and February 2023 to progress individual actions prior to the first formal meeting of the full group on 8 March 2023. **Working Group 2** *Led by:* Prof AJ McKnight, Dr Gillian Rea and Dr Alison Muir *Actions:* Rare Diseases Registry (Action 4), Pathways (Action 8) and Improve access to drugs & treatments (Action 11) and Improve access to rare disease specialist teams (Action 12). WG2 actions focus on improving the identification and treatment of rare diseases, as well as providing information about, and access to, specialist teams, with sub-groups taking forward specific pieces of work. The WG2 stakeholders include representatives from Queens University Belfast, DoH and Social Care Trusts and the National Institute for Health and Care Excellence (NICE). **Working Group 3** *Led by:* Dr Stephanie Duguez (Ulster University) and Dr Marian Traynor (QUB) (co-leads) *Actions:* Education & Training (Action 5) and Awareness Raising (Action 6) Stakeholder membership includes representatives from Queens University Belfast, Ulster University, the Open University, DoH and the NIRDP. **Working Group 4** *Led by:* Dr Julie McCarroll, R&D Division, Public Health Agency (PHA) *Actions:* Research (Action 13) Membership of WG4 includes representatives from Queen's University Belfast, Ulster University, University College Dublin, DoH, HSC Trusts, the PHA and the Northern Ireland Clinical Research Network (NICRN). **Working Group 5** *Led by:* Patrick Toland (NIRDP) and Finola McGrady (DoH)

	Actions: Rare Disease Champion (Action 14) WG5's membership includes representatives from the DoH and the NIRDP.
Funding model	*Note: Funding model not described. Descriptions of funding challenges extracted below.* As this is the first year of a five-year Action Plan, much of NIRDIG's early work focused on refining the parameters and tasks within each of the high-level actions, considering costings for actions, scoping rare disease research opportunities and developing options and research papers for discussion. This has set the groundwork for future years of the Action Plan and will help ensure we are in the strongest position possible to bid for future funding, should that become available. Each Working Group agreed a Terms of Reference and work plan for Year 1 and beyond and has been working hard throughout the first year to progress actions despite a lack of dedicated resource and funding. **CHALLENGES** The absence of a fully functioning Executive, along with associated budgetary and planning issues, continues to hinder progress in many areas across health and the NI Rare Diseases Action Plan is no exception. The Department is projecting a funding gap of some £764 million for the 2023/24 financial year and the current priority is to mitigate where possible both the immediate impact on frontline services and long-term irreversible consequences for the health and care system. Unfortunately, like all other NI departments, the DoH is trying to balance its responsibilities to live within the limited budget available, act in the public interest and safeguard services. The lack of confirmed recurrent funding is constraining not only the action outputs and out-workings of the Working Groups, but also the ability to make effective progress at pace. Currently in NI, there are a number of large Strategic Programmes and Projects taking forward the HSC Transformation agenda. Whilst some of these will inevitably define the feasibility of some rare diseases actions (for example those that involve encompass) and effective input is required at design stage, the available expertise is currently over-stretched and under competing time and work priorities. As a result, it was pragmatic to set up a number of sub-groups and smaller meetings to enable important work to progress that would inform relevant outcomes. This was apparent within WGs 1 and 2, where alternative approaches were required to progress milestones; for the most part this has worked well. However, opportunities to partake in wider UK and European research studies with potential associated funding have been made more difficult by the demanding time commitments commanded by the projects. We remain sincerely thankful to our NIRDIG members and wider Working Group colleagues for the continued time, effort and drive they contribute to the wider Rare Diseases agenda.
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	*See Action 3.*
Personalised medicine, genomics, genetic counselling	*See Action 2.*

Models of care/care pathways	*See Actions 1, 7, 8, 9, 12.*
Workforce	*See Actions 5 and 6.* The five NIRDIG Working Groups have been firmly established, led by members of NIRDIG with representation from NIRDP, as well as stakeholders from across clinical practice, academia, commissioners, research and policy. Each Working Group agreed a Terms of Reference and work plan for Year 1 and beyond and has been working hard throughout the first year to progress actions despite a lack of dedicated resource and funding. The quality of progress made to date is testament to the commitment and drive of our NIRDIG and Working Group members to deliver for the Rare Disease population in Northern Ireland. The appointment of both an Adult and a Paediatric Rare Diseases Clinical Lead consultant post is a major achievement. These posts will provide clinical leadership, advice and input to NIRDIG and to the implementation of actions, and will facilitate better communication and awareness-raising of rare diseases within the HSC. Recruitment for an adult rare disease/specialist service manager to support the clinical post is also planned. Throughout the year, there has been ongoing collaboration with training organisations across the UK and Ireland to enhance rare disease healthcare education and training via webinars and workshops, as well as work with Ulster University's School of Medicine to develop a rare diseases Student Selective Component for the undergraduate medical curriculum to help promote inclusion of rare diseases in teaching programs here, with the aim to continue this action into the long term.
European Reference Networks	Not mentioned.
EU alignment and participation	**Next steps** We will continue to seek out any and every opportunity to raise awareness of rare diseases and further work to build cross-border partnerships with counterparts in Ireland, as well as Europe, will also benefit rare diseases communities locally, nationally and internationally
Health information (including rare disease registries)	*See Actions 1, 4, 10, 12.* Other key areas of progress over the Action Plan's first year include linking with encompass on the new electronic patient record system/digital integrated healthcare record that will replace NI's outdated systems, and Digital Health & Social Care NI (DHSCNI) on the delivery of its Patient Portal and how it could benefit rare diseases nationally and internationally in the long term; reviewing the existing NI rare diseases coding infrastructure to inform the development of a NI Rare Diseases Registry; and work towards developing guiding principles for healthcare professionals around the transition journey of a rare disease patient moving from paediatric to adult services.
Orphan medicines	*See Action 11.*
Rare disease research	*See Action 13.*

	There has also been extensive work in the rare diseases research arena to apply for funding from external organisations, as well as active participation in several UK-wide research groups including a Rare Disease Research Landscape project and a UK Rare Disease International Mirror Action Group.
Alignment beyond the healthcare sector	*See Actions 6 and 9.*
Any additional information (for example, background to the strategy or strategy development)	Throughout 2021, the NIRDIG worked with stakeholders to develop a NI Action Plan in consultation with the rare disease community and informed by work previously undertaken by the NIRDP, to identify priorities for the rare disease population in NI. An online public engagement event in September 2021 produced stakeholders' top ranked actions under each UK Framework Priority. Informed by stakeholders' priorities, NIRDIG met regularly to develop the Year 1 actions for the NI Action Plan. This included presenting the draft actions to a stakeholder Focus Group organised by the NIRDP to consider, discuss and assess whether these actions met stakeholder expectations. Eleven rare disease conditions were represented at the Focus group and the feedback was positive, with stakeholders confirming they were content with the Year 1 actions and encouraged by the progress made so far. A key strength of NI's Action Plan is the extensive stakeholder engagement before and during the development of the Plan. It was designed to be meaningful, helpful and deliverable, and will be a living document to be reviewed annually, with actions closed, amended or added as required to encourage flexibility and autonomy for working groups to progress actions as the work evolves and new priorities emerge.

Key: APG: All-Party Group; CARDRISS: Congenital Anomaly and Rare Disease Registration and Information System Scotland; CARIS: Wales' Congenital Anomaly Register and Information Service; CPMS: Central Portfolio Management System; CTRIC: Clinical Translational Research and Innovation Centre; CPD: continuous professional development; DHSCNI: Digital Health and Care NI; DoH: Department of Health; EAMS: Early Access to Medicines Schemes; ECR: Extra Contractual Referral; GB: Great Britain; GDPR: General Data Protection Regulation; HSC: Health and Social Care; IFNA: International Family Nursing Association; IFR: Individual Funding Request; IMF: Innovative Medicines Fund; MLA: Member of the Legislative Assembly; MM: Musketeers Memorandum; NCARDRS: National Congenital Anomaly and Rare Disease Register; NI: Northern Ireland; NICE: National Institute for Health and Care Excellence; NICRF Northern Ireland Clinical Research Facility; NICRN: Northern Ireland Clinical Research Network; NICSM: Northern Ireland Centre for Stratified Medicine; NICTN: Northern Ireland Cancer Trials Network; NICTU: Northern Ireland Clinical Trials Unit; NIHR: National Institute for Health and Care Research; NIRADCAR: NI Rare Disease and Congenital Abnormality Registry; NIRDIG: Northern Ireland Rare Disease Implementation Group; NIRDP: Northern Ireland Rare Diseases Partnership; PHA: Public Health Agency; QUB: Queen's University Belfast; RAiN: All Ireland Rare Disease Inter-Disciplinary Research Network; RD: Rare Diseases; RDAG: Rare Diseases Advisory Group; RD-CaST-NI: Online Rare Disease Carer Support Tool in Northern Ireland; RDI: Rare Diseases Ireland; RDRL: Rare Diseases Research Landscape; RELAMC: Latin American Congenital Anomaly Network; RoI: Republic of Ireland; SENAC: Special Educational Needs Advice Centre; SSCAN: Sub-Saharan African Congenital Anomaly Network; S SWAN: Syndrome Without A Name; UK: United Kingdom; WG: working group.

Table B21. Data extracted for Portugal (Integrated strategy 2015 - 2020)

Portugal	Strategy information
Author(s) **Title**	Direção-Geral de Saúde Integrated Strategy for Rare Diseases 2015-2020[35]
Timeline	2015-2020
Overall aim(s)	The Integrated Strategy for Rare Diseases, based on an inter-ministerial, inter-sectoral and inter-institutional cooperation, which makes a complementary use of medical, social, scientific and technological resources, has as mission the development and improvement of [*the strategic priorities listed below*].
Themes and or priorities	**Strategic priorities** 1. Coordination of care 2. Access to early diagnosis 3. Access to treatment 4. Clinical and epidemiological information 5. Research 6. Social integration and citizenship.
Targets (if specified) and measurement method(s) (where available)	*Not mentioned.*
Implementation action(s), lead(s) and key performance indicator(s)	**Theme 1. Coordination of care** 1. Improve inter-ministerial, inter-sectoral and inter-institutional coordination of care, based on the complex needs of patients and their caregivers, and on the better use of national and regional resources, organising a coordinated approach of clinical and social services of both general and specialised support, by means of integrated plans of personal care. 2. Improve the offer of therapeutic, rehabilitation and diagnosis, and social inclusion interventions, which should be fast, effective, equitative and sustainable. 3. Design and implement integrated care, clearly defined, accessible and effective. 4. Define referral criteria for highly specialised centres. 5. Promote ways of joint work between patients and their families, their representing associations and supporting professionals, together with research and industry, in order to obtain better outcomes and benefits for individuals with rare diseases. **Theme 2. Access to early diagnosis** 1. Promote access equity to early diagnosis and treatments based on scientific evidence, through specialized clinical centres. 2. Define early diagnosis criteria for rare diseases. 3. Improve the identification of individuals with an increased, individual, familiar or geographic risk, given the probability of being carriers of specific hereditary diseases, namely through the implementation of common acting protocols. 4. Design cost-effective national programme proposals for the screening of rare diseases, based on the scientific evidence, internationally recognized as robust, on the economical evaluation and on the concrete treatment possibilities. 5. Improve the graduate and post-graduate professional training in rare diseases.

	6. Implement clinical guidelines on genetic testing prescription, promote the quality of medical genetic laboratories and, furthermore, improve the access to genetic testing for hereditary diseases. **Theme 3. Access to treatment** 1. Improve the access to early treatment by means of surgery, drugs or nutrition of serious rare diseases. 2. Implement adequate proceedings, both transparent and robust, for evaluation of cost-benefit innovating therapeutics for rare diseases. 3. Improve the information on new, available therapeutics. 4. Implement the systematic production of individual care plans after the diagnosis, based on evidence describing the expected course of the disease and also establishing the responsibilities of the several institutions and professionals involved in care provision. 5. Promote the use of telemedicine and information technologies as aid tools to the coordination of care, with the purpose of giving a better and faster access to merged specialized services, regardless of the geographical area where those services are located. 6. Cooperate in the identification and in the proposal for recognition of national Expertise Centres for rare diseases and further promote their integration in European reference networks. **Theme 4. Clinical and epidemiological information** 1. Promote the systematic use of the European information system Orphanet, embracing it as the reference portal and credible information source about rare diseases, their characteristics, diagnosis and treatment possibilities. 2. Design national registries of rare diseases, specifically through precise methods and genetic information gathering tools that allow incidence and prevalence calculations, which sustain the national strategic plan and the need to resort to European or international cooperation. 3. Increase the epidemiological, clinical and economic data reliability. 4. Develop at a national, European and international level, the share of information, knowledge, good practices and experience, in terms of diagnosis and treatment of rare diseases. **Theme 5. Research** 1. Promote research through collaborative activity amongst health and social services with the scientific and academic community, and with the industry. 2. Promote patients' participation in every stage of the research process, through the awareness and availability of accurate, adequate and helpful information, respecting the law and its dignity, 3. Improve the connection between research and the care provided to patients, thus promoting a culture of innovation. 4. The fastest access to care based on evidence. 5. Create partnerships in the scope of research to identify development opportunities for new drugs, which will help to improve the treatment and the evolution of the most common rare diseases. 6. Promote European and international cooperation in basic and translational research, mainly in the scope of extremely rare diseases. **Theme 6. Social inclusion and citizenship** 1. Develop training and education programmes for the health and social sector professionals, which will help their empowerment in the identification, treatment and rehabilitation of rare diseases. 2. Encourage active cooperation of patients' associations of rare diseases in the definition of integrated responses and in their achievement.

	3. Empower individuals with rare diseases and their caregivers, through the support from a coordinated and complementary action of patients' associations and - when relevant – through the satisfaction of special educational needs of those patients.
Governance and organisational structures	The Strategy is coordinated by an inter-ministerial commission, presided by the Director-General of Health, which sets out its functioning rules, and it is composed by the following members: a) One representative of the Directorate-General of Health b) One representative of the National Institute of Health, Dr. Ricardo Jorge c) One representative of the Central Administration of the Health System d) One representative of the National Authority for Medication and Health Products e) One representative of the Social Security Institute f) One representative of the National Institute for Rehabilitation g) One representative of the Foundation for Science and Technology h) One representative of the Directorate-General of Education, in the area of special educational needs.
Funding model	*Not mentioned.*
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	*See 'Access to early diagnosis', points 3 and 4.*
Personalised medicine, genomics, genetic counselling	*See 'Access to early diagnosis', point 6; Clinical and epidemiological information', point 2.* It should be underlined that medical genetics is inextricably linked to the diagnosis of rare diseases, due to the true outburst of new know-ledge and technology, especially in the area of molecular genetics, which is transversal to all medical fields and has opened new opportunity windows to better understand these diseases.
Models of care/care pathways	*See 'Coordination of care', points 1 to 5; 'Access to early diagnosis', points 1 and 2; Access to treatment', points 1, 4 and 5.*
Workforce	*See 'Access to early diagnosis', point 5; Social inclusion and citizenship', point 1.* The mere fact that these diseases are rare means that doctors, nurses, therapists, and pharmacists, as well as social assistants and teachers, often do not have the necessary information that would help them to adequately refer patients and their caregivers, amongst the possible and available responses. Thus, it is necessary to ensure that doctors are aware of the possibility of verifying a rare disease in a patient, even though they may not have the due competences to perform a specific diagnosis, since that they do not need to have an extensive knowledge about each of these diseases. Furthermore, efforts should be made, to enable all medical and multi-professional specialties the access to a general knowledge about rare diseases, so that they may, whenever necessary, promptly refer their patients to specialised or Expertise Centres.

European Reference Networks	*See 'Access to treatment', point 6.* Many doctors in clinical hospital services have acquired competences in specific diseases or groups of rare diseases, meaning that it is important to develop and assure that they have the necessary resources so that they may be identified as Expertise Centres for rare diseases, and eventually linked to European networks that may be created.
EU alignment and participation	*See 'Clinical and epidemiological information', points 1, 2 and 4; Research', point 6.*
Health information (including rare disease registries)	*See 'Access to treatment', point 5; 'Clinical and epidemiological information', points 1 to 4.* The use of new information technologies, as enablers for the said communication, means - increasingly more - that patients may access remotely to highly differentiated virtual services of specialists who are geographically distant from one another, thus reducing the need for dislocation of patients.
Orphan medicines	*See 'Access to treatment', points 1 to 3; Research', point 5.*
Rare disease research	*See 'Access to treatment', point 2; 'Research', points 1 to 6.*
Alignment beyond the healthcare sector	*See 'Coordination of care', points 1 and 2; 'Social inclusion and citizenship', points 1 to 3.*
Any additional information (for example, background to the strategy or strategy development)	**Definition of rare disease** In the European Union, diseases having a prevalence inferior to 5 cases for every ten thousand persons, are considered rare diseases, and occasionally also referred to as orphan diseases.

Table B22. Data extracted for Portugal (Annual Plan 2016).

Portugal	Strategy information
Author(s) **Title**	Directorate General for Health (DGS) Annual Plan 2016 – Integrated Strategy for Rare Diseases 2015-2020[36]
Timeline	2016
Overall aim(s)	…for the year 2016, all activities will have as their main objective the combating the vulnerability of this population group, through reducing the dispersion of information about these diseases, increased access to diagnostic and therapeutic interventions, better referral in the health system and greater health literacy for patients, families and caregivers.
Themes and or priorities	**Strategic priorities** 1. Coordination of care; 2. Access to early diagnosis; 3. Access to treatment; 4. Clinical and epidemiological information; 5. Research; 6. Social integration and citizenship.
Targets (if specified) and measurement method(s) (where available)	*See 'Products' listed below.*
Implementation action(s), lead(s) and key performance indicator(s)	*Planned activities and corresponding Products listed for each strategic priority.* **Theme 1. Coordination of care** ▪ **Planned activity:** Monitor the status of the provision of diagnostic, therapeutic, rehabilitation and social inclusion interventions. *Product*: Report mapping the provision of care. ▪ **Planned activity:** Standardization of clinical and organisational practice. *Products*: ○ Standard defining criteria for referring rare patients to reference centres already recognised by the Ministry of Health. ○ Standard itinerary aimed at families in the areas identified for Reference Centres. ▪ **Planned activity:** Satisfaction monitoring *Product*: Survey design and budgeting to assess the degree of satisfaction of people with rare diseases with the organisation of services (health, education, social sector) in response to their needs. **Theme 2. Access to early diagnosis** ▪ Carry out situation diagnosis on early diagnosis. *Product*: Report with recommendations. ▪ Standardisation of clinical and organisational practice. *Product*: Clinical standard on prescribing genetic tests. **Theme 3. Access to treatment**

	▪ Study an integrated intersectoral care model. *Product*: Report with a proposal for an integrated intersectoral care model. ▪ Disclose Information about Rare Diseases. *Products*: o Communication plan on rare diseases aimed at the educational community. o Update of the Orphanet portal with relevant information about existing treatments. o Outline guidelines for nutritional management in hereditary metabolic diseases within the scope of Reference Centres. **Theme 4. Clinical and epidemiological information** ▪ Design national registry of rare diseases. *Product*: Database model and IT platform to be made available to national reference centres for adaptation to each pathology and possible inclusion in relevant European networks. ▪ Improve the level of training of professionals who support rare disease patients. *Product*: Seminar in February 2017. **Theme 5. Research/Investigation** ▪ Identification of ongoing research in Portugal on rare diseases. *Products*: o Preparation of scientific meeting. o Report on ongoing research initiatives and their mapping with reference centres. o Outline research agenda for rare diseases. **Theme 6. Social integration and citizenship** ▪ Support schools in the integration of children with rare diseases. *Product*: Raise awareness among entities that provide family support to organise responses aimed at students with rare diseases. ▪ Identify the needs of patient associations. *Product*: Listening to patient associations.
Governance and organisational structures	During the preparation of the 2016 Annual Plan to operationalize the priorities set out in the Integrated Strategy for Rare Diseases 2015-2020, the following partners were invited to participate: ▪ Professional Orders in the Health area ▪ Associations that represent patients with rare diseases ▪ National Association of Portuguese Municipalities ▪ National Association of Parishes ▪ Social Sector partners. Therefore, this Annual Plan-2016…results from the commitment of the different representatives who make up the interministerial commission and the contributions of the Order of Pharmacists, Order of Nutritionists, Order of Nurses, Portuguese Alliance of Rare Disease Associations, Raríssimas Association and National Confederation of Solidarity Institutions (União das Misericórdias Portuguesas, União das Mutualidades and National Confederation of IPSS – CNIS).

Funding model	*Not mentioned.*
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	*Not mentioned.*
Personalised medicine, genomics, genetic counselling	*See 'Access to early diagnosis'.*
Models of care/care pathways	*See 'Coordination of care', 'Access to early diagnosis' and 'Access to treatment'.*
Workforce	*See 'Access to treatment' (Communication plan on rare diseases aimed at the educational community);* *'Clinical and epidemiological information' (seminar for professionals who support patients with rare diseases)*
European Reference Networks	As the recognition of Reference Centres is a national policy of global response to various areas of activity and considering that there is a great diversity of rare diseases, the interministerial commission plans to focus its main initiatives in 2016 on clinical areas, for which there are already in the process of official recognition (Ordinance no. 194/2014 of September 30) The Reference Centres, namely: rare paediatric cancers (applications under analysis), hereditary metabolic diseases (applications under analysis) and paramyloidosis (2 centres already recognized by the Ministry of Health in 2015).
EU alignment and participation	*Not mentioned.*
Health information (including rare disease registries)	*See 'Clinical and epidemiological information' (Design registry of rare diseases).* During 2016, we intend to leverage the macro and transversal initiative of conceptualization of a single intersectoral registry of rare diseases in Portugal. This registry must guarantee interoperability between different information systems relevant to monitoring people with these diseases, guaranteeing the ethical principles associated with confidentiality and processing of personal data.
Orphan medicines	*See 'Access to treatment' (Update of the Orphanet portal).*
Rare disease research	*See 'Research' activity.*
Alignment beyond the healthcare sector	*See 'Coordination of care' (Satisfaction monitoring) and 'Social integration and citizenship' activities.*

Any additional information (for example, background to the strategy or strategy development)	N/A.

Key: N/A: Not applicable.

Note: The information in this table was extracted from a version of the original document translated to English using Google Translate.

Table B23. Data extracted for Portugal (Annual Plan 2017).

Portugal	Strategy information
Author(s) **Title**	Ministry of Health and Directorate General for Health (DGS) Annual Plan 2017 – Integrated Strategy for Rare Diseases 2015-2020[37]
Timeline	2017
Overall aim(s)	…for the year 2017, all activities will have as their main objective the combating the vulnerability of this population group, through reducing the dispersion of information about these diseases, increased access to diagnostic and therapeutic interventions, better referral in the health system and greater health literacy for patients, families and caregivers
Themes and or priorities	**Strategic priorities** 1. Coordination of care; 2. Access to early diagnosis; 3. Access to treatment; 4. Clinical and epidemiological information; 5. Research; 6. Social integration and citizenship.
Targets (if specified) and measurement method(s) (where available)	*See 'Products' listed below.*
Implementation action(s), lead(s) and key performance indicator(s)	*Planned activities and corresponding Products listed for each strategic priority.* **Theme 1. Coordination of care** **Activities planned for 2017** ▪ Identification of the geographic areas most in need of support for people with a rare disease. ▪ Proposal for optimising local and regional responses to support people with rare diseases. *Product*: Proposal for a manual design of Support for People with a Rare Disease, to optimise the responses available locally. ▪ Conclusion of Clinical Standards with the definition of criteria for referring people with rare diseases to Reference Centres already recognised by the Ministry of Health. *Product*: Itinerary aimed at families for Reference Centres. ▪ Consultation with reference centres to help identify local care needs. *Product*: Preparation of a proposal to decentralise responses to people with rare diseases, with the aim of facilitating access and equity in available treatments. ▪ Implementation of the satisfaction survey aimed at people with rare diseases. *Product*: Report with the results and recommendations resulting from the survey. ▪ Disclosure of the Rare Disease Person Card (CPDR). *Products*: ○ Manual for assigning CPDR to users. ○ Participation in the "Portugal eHealth Summit" event.

	Theme 2. Access to early diagnosis **Activities planned for 2017** ▪ Organisation of an international symposium on neonatal screening for rare diseases, with a view to improving the qualifications of HR working in this field. *Product*: Multidisciplinary meeting on the relevance of early diagnosis. ▪ Conclusion of the standard defining the referencing criteria for carrying out genetic tests. *Product*: Publication of the standard. **Theme 3. Access to treatment** **Activities planned for 2017** ▪ Characterisation of existing responses in Reference Centres for rare diseases. *Product*: Dissemination (Orphanet national website, leaflet) of the answers that the Reference Centres provide to people with a rare disease. ▪ Monthly update of Orphanet's national portal with all national and international initiatives of interest and relevance for those interested in rare diseases. *Product*: Monthly update of Orphanet's national portal with relevant information about: – Existing treatments (Orphan medicines other medicines) – Clinical trials – Research projects – Relevant scientific publications – Laboratories – Patient associations. **Theme 4. Clinical and epidemiological information** **Activities planned for 2017** ▪ Contribute to the design of the national registry system for rare diseases *Product*: Identification of the number of people with a rare disease, with issuance of CPDR, stratified by areas and rare diseases ▪ Improve the level of training of professionals linked to the area of education who support people with rare diseases. *Product*: Seminar for the area of education. **Theme 5. Research** **Activities planned for 2017** ▪ Organisation of an international scientific meeting on modern research trends in rare diseases. *Product*: Scientific meeting. **Theme 6. Social integration and citizenship** **Activities planned for 2017** ▪ Develop actions with different partners in society who, in their daily activities, are asked to provide support to patients with rare diseases and their families.

	Products: ○ Meeting with the presidents of school groups to raise awareness of the need for training for CAF assistants and monitors who accompany children with rare diseases. ○ Design of a proposal for funding applications for local responses to support people with a rare disease.
Governance and organisational structures	During the preparation of this Plan, to operationalise the priorities set out in the Integrated Strategy for Rare Diseases 2015-2020, the following partners were invited to participate: Professional Orders in the area of Health; Associations that represent patients with rare diseases; National Association of Portuguese Municipalities; National Association of Parishes and Social Sector partners.
Funding model	*Not mentioned.*
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	*See 'Access to early diagnosis'.*
Personalised medicine, genomics, genetic counselling	*See 'Access to early diagnosis'.*
Models of care/care pathways	*See 'Coordination of care', 'Access to early diagnosis' and 'Access to treatment'.*
Workforce	*See 'Clinical and epidemiological information' (seminar).*
European Reference Networks	*Not mentioned.*
EU alignment and participation	*Not mentioned.*
Health information (including rare disease registries)	*See 'Coordination of care' (Rare Disease Person Card), 'Clinical and epidemiological information' (national registry).* The commitment made for 2017 aims to facilitate the conceptualization of a single intersectoral registry of rare diseases in Portugal. This registry must guarantee interoperability between different information systems relevant to monitoring people with these diseases, guaranteeing the ethical principles associated with confidentiality and processing of personal data.
Orphan medicines	*See 'Access to treatment' (Update of the Orphanet portal).*

Rare disease research	*See 'Research' activity.*
Alignment beyond the healthcare sector	*See 'Coordination of care' (satisfaction survey) and 'Social integration and citizenship'.*
Any additional information (for example, background to the strategy or strategy development)	*N/A.*

Key: CPDR: Rare Disease Person Card; N/A: not applicable.

Note: The information in this table was extracted from a version of the original document translated to English using Google Translate.

Table B24. Data extracted for Portugal (Annual Plan 2018).

Portugal	Strategy information
Author(s) **Title**	Ministry of Health and Directorate General for Health (DGS) Annual Plan 2018 – Integrated Strategy for Rare Diseases 2015-2020[38]
Timeline	2018
Overall aim(s)	The objective of this Strategy is to ensure that people with a rare disease have better access and quality of healthcare and treatment, based on the evidence that science has been producing and greater speed and variety of social responses adapted to each case.
Themes and or priorities	**Strategic priorities** 1. Coordination of care; 2. Access to early diagnosis; 3. Access to treatment; 4. Clinical and epidemiological information; 5. Research; 6. Social integration and citizenship.
Targets (if specified) and measurement method(s) (where available)	*Not mentioned.*
Implementation action(s), lead(s) and key performance indicator(s)	*Planned activities and corresponding Responsible Entities listed for each strategic priority.* **Theme 1. Coordination of care** **Activities planned for 2018** ▪ Identification of local and regional responses to support people with a rare disease. ▪ Publication and updating of the Manual of Support for People with a Rare Disease. *Responsible Entities*: ○ Directorate General for Health (DGS) ○ INFARMED ○ Central Administration of the Health System (ACSS) ○ National Institute of Rehabilitation (INR) ○ Social Security Institute (ISS) ○ Directorate General of Education (DGE) ○ National Institute of Health Dr. Ricardo Jorge (INSA) ○ Science and Technology Foundation (FCT) **Theme 2. Access to early diagnosis** **Activities planned for 2018**

	▪ Transfer of next generation sequencing (NGS) technology for the diagnosis of rare diseases with no known cause, reducing the time to etiological diagnosis. *Responsible Entity*: INSA. **Theme 3. Access to treatment** **Activities planned for 2018** ▪ Implementation of the questionnaire for the national mapping of health services responses aimed at people with rare diseases. *Responsible Entities:* o DGS o INFARMED o ACSS o INSA **Theme 4. Clinical and epidemiological information** **Activities planned for 2018** ▪ Orphanet portal update. *Responsible Entity*: DGS ▪ Reflection document on the variables to be considered in a national rare disease registry. *Responsible Entities:* o INSA o DGS o INFARMED o ACSS **Theme 5. Research/Investigation** **Activities planned for 2018** ▪ Design of the agenda for Research, Development & Innovation in Rare Diseases. *Responsible Entities:* o FCT o INSA ▪ Survey of research projects under development in Rare Disease Reference Centres *Responsible Entities:* o INSA o DGS o INFARMED **Theme 6. Social integration and citizenship** **Activities planned for 2018** ▪ Training actions for teachers on the Health Education Framework. ▪ Training actions for teachers – For the development of an Inclusive School.

	▪ Promotion of debates in schools with students on the development of responsibility, citizenship and participation skills. *Responsible Entity:* DGE ▪ Publication of the Manual on the ISS website with all the Social Security assistance, and social responses that provide support to people with rare diseases. *Responsible Entity:* ISS
Governance and organisational structures	…an Interministerial Commission was set up to implement the Integrated Strategy for Rare Diseases 2015-2020. Within the scope of the powers attributed to this Interministerial Commission, the proposal for the 2018 annual plan is presented.
Funding model	Not mentioned.
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	*Not mentioned.*
Personalised medicine, genomics, genetic counselling	*See 'Access to early diagnosis'.*
Models of care/care pathways	*See 'Coordination of care', 'Access to early diagnosis' and 'Access to treatment'.*
Workforce	*See 'Social integration and citizenship' (training for teachers).*
European Reference Networks	*Not mentioned.*
EU alignment and participation	*Not mentioned.*
Health information (including rare disease registries)	*See 'Clinical and epidemiological information'.*
Orphan medicines	*See 'Access to treatment' (Update of the Orphanet portal).*

Rare disease research	*See 'Access to treatment' and 'Research'.*
Alignment beyond the healthcare sector	*See 'Coordination of care' (Manual of Support for People with a Rare Disease) and 'Social integration and citizenship'.* This National Strategy is a pioneer at European level and replaces the old National Program for Rare Diseases, which was unable to respond to the needs of people with a rare disease, as its scope of action goes beyond the Health sector.
Any additional information (for example, background to the strategy or strategy development)	N/A.

Key: DGS: Directorate General for Health; INFARMED, ACSS: Central Administration of the Health System; INR: National Institute of Rehabilitation; ISS: Social Security Institute; DGE: Directorate General of Education, INSA: National Institute of Health Dr. Ricardo Jorge; FCT: Science and Technology Foundation.
Note: The information in this table was extracted from a version of the original document translated to English using Google Translate.

Table B25. Data extracted for Portugal (Annual Plan 2019).

Portugal	Strategy information
Author(s) **Title**	Ministry of Health and Directorate General for Health (DGS) Annual Plan 2019 – Integrated Strategy for Rare Diseases 2015-2020[40]
Timeline	2019
Overall aim(s)	…for the year 2019, all activities will have as their main objective the combating the vulnerability of this population group, through reducing the dispersion of information about these diseases, increased access to diagnostic and therapeutic interventions, better referral in the health system and greater health literacy for patients, families and caregivers.
Themes and or priorities	**Strategic priorities** 1. Coordination of care 2. Access to early diagnosis 3. Access to treatment 4. Clinical and epidemiological information 5. Research 6. Social integration and citizenship.
Targets (if specified) and measurement method(s) (where available)	*Not mentioned.*
Implementation action(s), lead(s) and key performance indicator(s)	*Abbreviations: Directorate-General of Health (DGS); National Institute of Health Doctor Ricardo Jorge, IP (INSA); Central Administration of the Health System, IP (ACSS); National Authority for Medicines and Health Products, I. P (INFARMED); Social Security Institute, IP (MSS National Institute for Rehabilitation, IP (INR); Foundation for Science and Technology, IP (FCT); Directorate-General for Education in the area of special educational needs (DGE)* *Planned activities and corresponding Responsible Entities listed for each strategic priority.* **Theme 1. Coordination of care** **Activities planned for 2019** ▪ Develop informative/educational material on the services/care available for people with rare diseases, with the involvement of associations of people with rare diseases and health professionals. ○ *Responsible Entities*: All entities that are part of the Integrated Strategy for Rare Diseases ▪ Monitor the work of the treatment and monitoring committees for rare diseases. ○ *Responsible Entities*: DGS; ACSS; INFARMED ▪ Analyse the work and articulation mechanisms in the provision of care. ○ *Responsible Entity*: ACSS ▪ Analyse and present proposals for the development of a reference centre for rare diseases. ○ *Responsible Entities*: INSA; DGS; ACSS; INFARMED ▪ Promote meetings with patients' associations and their representatives. ○ *Responsible Entities*: All entities that are part of the Integrated Strategy for Rare Diseases

Access to early diagnosis
Activities planned for 2019

- Recognition of pulmonary arterial hypertension treatment centres.
  - *Responsible Entities*: DGS; MS
- Proposal for a screening program for example, normative circular on haemoglobinopathies
  - *Responsible Entity*: INSA
- Expansion of the current National Early Diagnosis Program (heel prick test) to include screening for sickle cell anaemia (sickle cell anaemia).
  - *Responsible Entity*: INSA
- Raise awareness among the Medical Association about the importance of training in rare diseases in the internship program of some medical specialties.
  - *Responsible Entity*: DGS
- Update of the standard on Prescription, Laboratory Execution and Information Processing of Genetic Tests related to Paediatric and Adult Health.
  - *Responsible Entity*: DGS
- Promote European Reference Networks within the scope of care provision.
  - *Responsible Entity*: DGS

Access to treatment
Activities planned for 2019

- Development of informative material on nutrition care in the area of Rare Diseases.
  - *Responsible Entities*: All entities that are part of the Integrated Strategy for Rare Diseases plus the Order of Nutritionists.
- Monitoring of international groups debating this matter and in which INFARMED is part, and if applicable to the national context.
  - *Responsible Entity*: INFARMED
- Integrate Patients and/or Representatives of Patients' Associations in the evaluations of new therapies/innovative therapeutic approaches in rare diseases (INCLUIR project).
  - *Responsible Entity*: INFARMED
- Develop drug presentation tools by disease.
  - *Responsible Entity*: INFARMED
- Promote meetings between Patients' Associations and the National Authority for Medicines and Health Products, INFARMED (INCLUDING project).
  - *Responsible Entity*: INFARMED
- Raise awareness in reference centres for implementing the individual care plan.
  - *Responsible Entities:* INSA; DGS; ACSS; INFARMED
- Identify the clinical areas and locations of the national health service (SNS) that could benefit from telemedicine resources, which contribute to greater and better access to care.
  - *Responsible Entities*: All entities that are part of the Integrated Strategy for Rare Diseases
- Survey of rare diseases in Portugal for which there is no organised response.
  - *Responsible Entities:* INSA; DGS; ACSS; INFARMED

	▪ Present a well-founded proposal for rare diseases, without an organised response in Portugal, for possible application to a reference centre. ○ *Responsible Entities:* INSA; DGS; ACSS; INFARMED **Clinical and epidemiological information** **Activities planned for 2019** ▪ Continued update of the Orphanet portal. ○ *Responsible Entity*: DGS ▪ Monitoring the implementation of the National Rare Disease Registry System based on the reflection made in 2018. ○ *Responsible Entities*: All entities that are part of the Integrated Strategy for Rare Diseases ▪ Hold a national day aimed at health professionals and users. ○ *Responsible Entities:* INSA; DGS; ACSS; INFARMED **Research** **Activities planned for 2019** ▪ Monitoring the implementation of the Research, Development & Innovation in Rare Diseases Agenda prepared in 2018. ○ *Responsible Entities: FCT;* INSA ▪ Carrying out awareness-raising actions involving researchers and associations. ○ *Responsible Entities:* FCT; INSA ▪ Initiatives to support the protection of intellectual property and innovation in the area of Rare Diseases, respecting the protection of people with a rare disease. ○ *Responsible Entities*: All entities that are part of the Integrated Strategy for Rare Diseases ▪ Initiatives to promote pre-clinical and clinical research associated with reference centres. ○ *Responsible Entities:* FCT; INSA ▪ Participation in EJPRD – European Joint Programme on Rare Diseases 2019-2024. ○ *Responsible Entities:* FCT; INSA ▪ Financial support for transnational research projects in the area of rare diseases through the Portuguese Representation at ERA-Net E-Rare. ○ *Responsible Entities:* FCT; INSA **Social integration and citizenship** **Activities planned for 2019** ▪ Publication of the Manual on the ISS website with all the Social Security Assistance services and social responses that provide support to people with rare diseases. ○ *Responsible Entity:* ISS ▪ Monitoring the implementation of Decree-Law 54/2018, of July 6 – Inclusive education Regional Meetings: training actions in school groups as requested; information sessions in Hospital Centres and Rehabilitation Centres, upon request; information sessions aimed at families. ○ *Responsible Entity:* DGE ▪ Organisation of events with patient associations.

	○ *Responsible Entities*: All entities that are part of the Integrated Strategy for Rare Diseases ▪ Regional Meetings within the scope of Curricular Flexibility. Decree-Law No. 55/2018, of July 6, in the subject Citizenship and Development, promoting the responsible and civic participation of students. ○ *Responsible Entity:* DGE
Governance and organisational structures	The interministerial Commission created to implement the Integrated Strategy for Rare Diseases 2015-2020, is made up of representatives from various bodies, and chaired by the Director-General of Health (DGS), namely: Directorate-General of Health (DGS); National Institute of Health Doctor Ricardo Jorge, IP (INSA); Central Administration of the Health System, IP (ACSS); National Authority for Medicines and Health Products, IP (INFARMED); Social Security Institute, IP (MSS) National Institute for Rehabilitation, IP (INR); Foundation for Science and Technology, IP (FCT); Directorate-General for Education in the area of special educational needs (DGE). During the preparation of the 2019 Annual Plan to operationalise the priorities set out in the Integrated Strategy for Rare Diseases 2015-2020, the following partners were invited to participate: Professional Orders in the Health area; Associations that represent patients with rare diseases; National Association of Portuguese Municipalities; National Association of Parishes and Social Sector partners. Thus, this Annual Plan-2019 for operationalising the priorities set out in the Integrated Strategy for Rare Diseases in the year 2015-2020 results from the commitment of the different representatives who make up the interministerial committee and the contributions of the Order of Pharmacists, Order of Nutritionists, Order of Nurses, Portuguese Alliance of Rare Disease Associations, and National Confederation of IPSS – CNIS (*IPSS = Private Institutions of Social Solidarity; CNIS = National Confederation of Solidarity Institutions*).
Funding model	*Not mentioned.*
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	*See 'Access to early diagnosis'.*
Personalised medicine, genomics, genetic counselling	*See 'Access to early diagnosis'.*
Models of care/care pathways	*See 'Coordination of care', 'Access to early diagnosis' and 'Access to treatment'.*
Workforce	*See 'Access to early diagnosis' (raise awareness with Medical Association), 'Social integration and citizenship' (training for teachers).*
European Reference Networks	*See 'Access to early diagnosis'.*

EU alignment and participation	*See 'Access to treatment' and Research' (EJPRD and E-Rare).*
Health information (including rare disease registries)	*See 'Clinical and epidemiological information'.*
Orphan medicines	*See 'Access to treatment' (Update of the Orphanet portal).*
Rare disease research	*See 'Access to treatment' (survey) and 'Research'.*
Alignment beyond the healthcare sector	*See 'Coordination of care' (Manual of Support for People with a Rare Disease) and 'Social integration and citizenship'.*
Any additional information (for example, background to the strategy or strategy development)	**Definition of rare disease** In Europe, a disease is considered rare when it affects 1 in every 2,000 people… *Note: Annual Plan 2019 makes reference to involvement of patient associations across a number of actions (not included to the same extent in previous Annual Plans).*

Key: DGS: Directorate-General of Health; IP (INSA) National Institute of Health Doctor Ricardo Jorge; ACSS: Central Administration of the Health System, IP; I. P (INFARMED): (MSS National Institute for Rehabilitation, IP (INR) National Authority for Medicines and Health Products; Social Security Institute, IP); FCT: Foundation for Science and Technology, IP; DGE: Directorate-General for Education in the area of special educational needs).
Note: The information in this table was extracted from a version of the original document translated to English using Google Translate.

Table B26. Data extracted for Portugal (2018 Annual Report).

Portugal	Strategy information
Author(s) **Title**	Directorate-General for Health (*Direção-Geral de Saúde*, DGS) 2018 Annual Report: Integrated Strategy for Rare Diseases 2015-2020[41]
Timeline	2018
Overall aim(s)	In this annual report, the activities developed by the inter-ministerial commission in the year 2018 were presented, in accordance with the strategic priorities defined in Order No. 2129-B/2015.
Themes and or priorities	**Strategic priorities** 1. Coordination of care 2. Access to early diagnosis 3. Access to treatment 4. Clinical and epidemiological information 5. Research 6. Social integration and citizenship.
Targets (if specified) and measurement method(s) (where available)	*Not mentioned.*
Implementation action(s), lead(s) and key performance indicator(s)	Following the implementation of the 2018 annual plan of the Integrated Strategy for Rare Diseases 2015-2020, activities falling within strategic priorities are the following: **Coordination of care** ▪ With the aim of publicising the resources, rights and benefits made available by public services to people with rare diseases throughout their life cycle, the support manual for people with rare diseases was published in all bodies that make up the Interministerial Commission. It is the intention of this committee to update this manual annually, in order to ensure it is up-to-date and useful. ▪ In the area of monitoring rare diseases, Order No. 1818/2018, dated 1 March, created the Coordinating Committee for the Treatment of Cystic Fibrosis Disease (CCTDFQ), whose mission is to monitor and monitor the treatment of this pathology. Order No. 2123/2018, of 28 February, appointed the members who make up the CCTDFQ, namely a doctor designated by each of the five Reference Centres recently created by Order No. 6669/2017, of 2 August, a member from the Central Administration of the Health System (ACSS), a member from the National Medicines Authority (INFARMED), one member of the General Directorate of Health (DGS) and two members of the Shared Services of the Ministry of Health, EPE (SPMS). ▪ Clinical standards were completed and published with the aim of implementing clearly defined, accessible and effective integrated care pathways, namely: ○ Standard 017/2018 – Referral of people with Congenital Coagulopathies ○ Standard 008/2018 – Diagnosis and follow-up of people with Tuberous Sclerosis in Paediatrics and Adults.

	▪ As the dissemination and implementation of the Card for People with a Rare Disease is an area of action prioritised by this strategy in 2018, the following actions were carried out: ○ Update of the DGS Standard that defines its issuance conditions, informing the possibility of the user being able to consult it in the Citizen Area of the National Service Portal of health. ○ Participation of DGS in the "Portugal eHealth Summit" event, disseminating updates on conditions for requesting the Rare Disease Card. **Access to early diagnosis** ▪ The Neonatal Screening, Metabolism and Genetics Unit of the Department of Human Genetics of the National Institute of Health Dr. Ricardo Jorge (INSA), started to make next generation sequencing of gene panels available for the molecular diagnosis of hereditary metabolic diseases. Next generation sequencing analysis allows the study of multiple genes simultaneously, which is much quicker and more economical than individual analysis of each gene. This strategy thus provides a high capacity for genetic diagnosis, even in rare diseases with no known cause, reducing the time to diagnosis. ▪ The National Early Diagnosis Programme (run at INSA) started to include cystic fibrosis (or mucoviscidosis) in the list of pathologies to be screened in the neonatal period. ▪ Recognising the difficulty of diagnosing many rare diseases that manifest at any stage of the life cycle, the General Directorate of Health published Standard 008/2018 regarding the Diagnosis and follow-up of people with Tuberous Sclerosis in Paediatrics and Adults. ▪ Continuing the work carried out in previous years to define criteria for the early diagnosis of rare diseases, Standard 007/2018 of the General Directorate of Health was published, which defines the conditions for Prescription, Laboratory Execution and Processing of Information for Genetic Tests related to Paediatrics and Adult Health, which are currently being updated in content. **Access to treatment** ▪ To improve access to early treatment of serious rare diseases, INFARMED approved eight orphan medicines in 2018, for one or more indications, one more than in 2017. During 2018, as part of the Horizon Scanning project, INFARMED requested approximately 200 companies in the pharmaceutical sector to send information about the financing requests they will submit until the end of 2019, for new active substances, new indications and first generics and biosimilar. With this request, it defined an innovation map for Portugal for the next two years, in order to establish priorities and speed up the entry into the market of new health technologies. By 2020, the submission of 38 new therapeutic indications corresponding to 32 medicines with orphan medicine status is expected, for the following therapeutic areas: Endocrinology; Genitourinary; Immunoallergology; Medicines used in transplantation; Nutrition and Metabolism; Ophthalmology; Oncology; Respiratory; Blood; and Central Nervous System. ▪ With the aim of improving information about new therapies available, INFARMED has been developing new tools that contribute to strengthening relationships with citizens and people with a disease through the dissemination of information on social networks, through the creation of the Include Project. The aim of this project is to expand the interaction of patients and or patient associations in the process of health technology assessment and other areas such as drug shortages, reporting of adverse reactions or counterfeit medicines; and, thus, to enable entities representing patients to become more informed about INFARMED's processes and for INFARMED to include the perspectives of person with diseases, their experiences, needs and preferences, as well as those of their caregivers and family members, in its processes and activities. Until the end of February 2018, citizens with a disease and or patient associations that represent them were able to submit their interest in participating in this project to INFARMED.

	▪ The Central Administration of Health Systems promotes the use of telemedicine and information technologies as assistance tools for care coordination, in order to provide better and faster access to concentrated specialised services, regardless of the geographic area where the services are located. ▪ With the intention of collaborating in the identification and proposal for recognition of national reference centres for rare diseases, INSA carried out a consultation of the medical community of rare diseases, which resulted in the preparation of a fundamental proposal for the opening of a tender for national reference centres, to be delivered to the National Commission for Reference Centres. **Clinical and epidemiological information** ▪ Following the functions assigned to the Orphanet national team, in accordance with "Orphanet Standard Operating Procedures", the actions developed by the Orphanet National Team contributed to updating the international database, facilitating access to information in the Portuguese language. These tasks were: o Review and translation of more than 1000 Rare Diseases according to the Orpha nomenclature o Participation in national events to publicise the Orphanet portal and database o Registration of more than 100 genetic tests available in Portugal, in the ORPHANET database o Identification and registration, in the Orphanet database, of hospital consultations addressed to rare patients and the respective national health service health professionals who carry them out o Registration in the Orphanet database of reference centres for rare diseases recognised in Portugal o Registration, in the Orphanet database, of national and regional rare patient associations. ▪ With the aim of contributing to the implementation of the national registry of rare diseases, the Interministerial Commission prepared a reflection document on the variables to be considered in a national registry of rare diseases, using as a reference a set of common data for the European Registry of Rare Diseases, presented by the European Commission – Joint Research Centre. **Research** ▪ Following consultation with the scientific community, professionals and associations of patients with rare diseases, a proposal for an agenda for research, development and innovation in rare diseases was presented. This proposal follows the Rare Diseases Symposium_2017, held at INSA in Lisbon on 15 December 2017, co-organised by INSA and the Foundation for Science and Technology with financial support from INSA and the Amélia de Mello Foundation. This event aimed to give visibility and stimulate scientific research in rare diseases. Contributions from Portuguese and foreign experts were presented to an audience of around 150 people, made up of members of the scientific community, health professionals, patient associations and representatives of the health products industry. One of the practical results of this initiative was the development and validation of the research, development and innovation agenda aimed at improving knowledge about rare diseases in the following areas: epidemiology, diagnosis, pathophysiological models and mechanisms, therapeutic approaches and resources for those living with these diseases. **Social integration and citizenship** ▪ With the intention of developing training, education and training programmes for health and social sector professionals to help build their capacity in relation to rare diseases, the Interministerial Commission proposed as training priorities for the years 2019-2020, within the scope of the Social Inclusion and Employment Operational Programme (for the North, Centre and Alentejo regions) and the Algarve Regional Operational Programme (for the Algarve region), the carrying out of an awareness-raising campaign for rare diseases aimed at health professionals. The specific objectives proposed for this action were: increase knowledge about the evolution of the diagnosis of

	rare diseases; raise awareness among health professionals about the difficulties experienced by people with rare diseases; publicise the resources available in Portugal for the diagnosis, treatment and monitoring of people with rare diseases. ▪ To encourage the active collaboration of associations of patients with rare diseases in defining integrated responses and implementing them, INFARMED and the National School of Public Health at Universidade Nova de Lisboa established a partnership within the scope of the "Include Project". The purpose of this partnership was to carry out training actions aimed at patient associations. The first action took place in November 2018. The participation of citizens with illnesses or their representatives is carried out on a case-by-case basis depending on the specificities of each consultation process. At this stage, the priority is to be involved in the health technology assessment process, namely in the contribution of the citizen to the identification of relevant measures of effectiveness and quality of life. ▪ The active collaboration of associations that represent people with rare diseases has been, over the years, a fundamental activity for defining and implementing integrated responses aimed at the needs of people with rare diseases. During 2018, more than 30 actions were carried out, aimed not only at people with rare diseases, but also at the scientific community and civil society. ▪ For the development of training, education and training programs for health professionals and the social sector, several training actions for trainers were carried out for the Development of an Inclusive School, following the publication of Decree-Law no. 54/2018, of 6 July. These actions had the participation of 130 teachers and took place in Braga, Porto, Chaves, Coimbra and Évora, with the objective of training teachers for training and its replication on the implementation of the new legal framework for inclusive education. ▪ With the publication of Decree-Law no. 55/2018, of 6 July, on curricular flexibility, and based on the National Strategy for Education for Citizenship and the Profile of Students Leaving Compulsory Education, training actions were carried out in Vila Nova de Gaia and Beja for around 30 teachers with the aim of training and or equipping teachers to replicate peer training in the use of the Health Education Framework, as a universal tool for the development of personal, cognitive and socio-emotional skills and promoting students' health literacy. ▪ At the beginning of the 2018/2019 academic year, joint teams were created and carried out workshops with Directors of School Groups, to implement these two Diplomas – Inclusive Education – Curriculum Flexibility and Education Strategy for School Citizenship. It is intended that these teams, made up of Technicians and Teachers, can cover all groups of schools in the country, which is why this work has been continued throughout the year. ▪ To empower people with rare diseases and their caregivers, the MAVI project (Model of Support for Independent Living) was presented. The Independent Living Support Model – Personal Assistance for people with disabilities foresees the existence of pilot projects for the period 2017-2020 that will be co-financed by Portugal 2020, within the scope of the Thematic Domain Social Inclusion and Employment. This project, despite not being exclusively aimed at people with rare diseases, contributes to increasing the functionality and quality of life of people with more disabling rare diseases.
Governance and organisational structures	See Integrated Strategy for Rare Diseases 2015-2020 and Annual Plan 2018. When comparing the activity plan designed for 2018 and the results demonstrated in this report, it appears that some of the planned activities were not implemented. However, it is also possible to verify that with the individual and collective contribution of all the organisations that make up this Interministerial Commission, it was possible to design and implement several activities that were not initially foreseen, but that are considered relevant for people with a rare disease.
Funding model	The absence of a specific budget allocated to the activities of the Integrated Strategy for Rare Diseases 2015-2020 and the impossibility of the entities involved being able to accept external financing from private, for-profit entities, is one of the biggest constraints on the implementation of the annual plans.

	In view of the above, the activities planned for 2019 should continue to be programmed within the strict domain of skills and resources available to the different partners of the Strategy, with possible limitations in the definition of some objectives.
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	*See 'Access to early diagnosis'.*
Personalised medicine, genomics, genetic counselling	*See 'Access to early diagnosis' and Clinical and epidemiological information'.*
Models of care/care pathways	*See 'Coordination of care', 'Access to early diagnosis' and 'Access to treatment'.*
Workforce	*See 'Clinical and epidemiological information' (seminar).*
European Reference Networks	*See Coordination of care', 'Access to treatment' and 'Clinical and epidemiological information' for references to Reference Centres.*
EU alignment and participation	*See 'Clinical and epidemiological information' (European Registry of Rare Diseases). Also under 'Social integration and citizenship', activities carried out by associations of people with rare diseases include links to European activities relating to Huntington's disease.*
Health information (including rare disease registries)	*See 'Coordination of care' (Card for People with a Rare Disease), 'Clinical and epidemiological information'.*
Orphan medicines	*See 'Access to treatment'.*
Rare disease research	*See 'Research'.*
Alignment beyond the healthcare sector	*See 'Coordination of care' and 'Social integration and citizenship'.*
Any additional information	N/A.

(for example, background to the strategy or strategy development)	

Key: CCTDFQ: Cystic Fibrosis Disease; ACSS: Central Administration of the Health System; MAVI project: Model of Support for Independent Living; ACSS: Central Administration of the Health System; INFARMED: National Medicines Authority; DGS: General Directorate of Health; SPMS: Shared Services of the Ministry of Health, EPE; INSA: National Institute of Health Dr. Ricardo Jorge.

Note: The information in this table was extracted from a version of the original document translated to English using Google Translate.

Table B27. Data extracted for Portugal (Interim Report 2017).

Portugal	Strategy information
Author(s) **Title**	Directorate-General for Health (*Direção-Geral de Saúde*, DGS) Interim Report on the Implementation of the Integrated Strategy for Rare Diseases 2015-2020: Year 2017[39]
Timeline	2017
Overall aim(s)	Within the scope of the powers attributed to this Interministerial Commission, the annual report on the implementation of the 2017 annual plan of the Strategy is presented.
Themes and or priorities	**Strategic priorities** 1. Coordination of care 2. Access to early diagnosis 3. Access to treatment 4. Clinical and epidemiological information 5. Research 6. Social integration and citizenship.
Targets (if specified) and measurement method(s) (where available)	*Not mentioned.*
Implementation action(s), lead(s) and key performance indicator(s)	Following the implementation of the 2017 annual plan of the Integrated Strategy for Rare Diseases 2015-2020, activities falling within strategic priorities are the following: **Coordination of care** ▪ With the aim of identifying the geographical areas most in need of support for people with a rare disease, different surveys were designed to be applied, in 2018, to the District Social Security Centres and the national Hospital Network, with the aim of mapping the responses of the different sectors that are part of the Integrated Strategy. ▪ A manual was created aimed at people with rare diseases, to be published in 2018, characterising the resources, rights and benefits provided by public services throughout the life cycle. Its publication and wide dissemination is the responsibility of the institutions that are part of the Interministerial Strategy. ▪ Completed and published clinical standards on the diagnostic approach and referral criteria for the Reference Centres already recognised by the Ministry of Health, in the following areas: ○ Paramyloidosis in adolescents and adults ○ Hereditary metabolic diseases in paediatrics and adults ○ Paediatric cancers. ▪ Although the activity plan foresees the consultation of Reference Centres to identify local care needs, this will take place when responding to the aforementioned surveys, analysing the information for these units separately. By collecting this information it will be possible to characterise the available response and list the greatest needs.

	▪ The implementation of the satisfaction survey aimed at people with rare diseases, planned as an activity to be implemented during 2017 by the National Institute for Rehabilitation, was not completed, because, despite the availability of funds in its budget for this activity, it was insufficient given the costs that this process entails. ▪ Several initiatives were carried out to increase the publicity of the Rare Diseases Person Card (RDPC), namely: o Update of DGS Standard No. 008/2014, extending the RDPC request to all public and private hospitals in the Health System and RARÍSSIMAS, with each institution being responsible for its promotion and implementation. This initiative resulted in an increase in the number of RDPCs requested and the number of new rare diseases coded during 2017. o Participation of DGS and ACSS in the "Portugal eHealth Summit" event, disclosing updates on the conditions for requesting the RDPC. o Information leaflet aimed at people with a rare disease, prepared by the DGS and published by all partners. **Access to early diagnosis** ▪ With the aim of making all health professionals aware of laboratory and clinical follow-up activities, but also the exchange of information between professionals and management bodies of the National Early Diagnosis Program and the Department of Human Genetics, two training sessions entitled "A Day with Early Diagnosis" took place at INSA, on 11 April 2017 and 21 November 2017. ▪ With the aim of facilitating access to early diagnosis of rare diseases in the context of the National Health Service, the Directorate-General for Health completed the standard on "Prescription, Laboratory Execution and Information Processing of Genetic Tests related to Health in Paediatrics and Adults", to be published in 2018. **Access to treatment** ▪ With the aim of publicising existing responses in reference centres for rare diseases, a publicity leaflet was prepared, available for download on the National Orphanet Portugal website. ▪ The monthly update of Orphanet's national portal with all national and international initiatives of interest and relevance in the area of rare diseases was a partially successful activity, since the maintenance and updating of the national page is constrained by technical difficulties in updating the website. ▪ To minimise this obstacle, the Directorate-General for Health, through its national Orphanet team, disseminated the systematic use of the European information system Orphanet, adopting it as a reference portal and source of credible information on rare diseases, their characteristics, diagnostic and treatment possibilities. To this end, efforts were made to adapt the information available on the international Orphanet portal to the Portuguese language. ▪ In 2017, continuing the process of recognising Reference Centres by the Ministry of Health, 10 new centres were created in the area of rare diseases; five related to Cystic Fibrosis and five related to Congenital Coagulopathies. It should be noted that generic incentive principles are applied to Reference Centres and, for certain pathologies, specific financing models, in order to promote exclusive activity in these units, which is intended to be of excellence. ▪ Within the scope of access to medicine, 14 orphan medicines were approved in Portugal in 2017. These medicines have a regulatory status assigned. They are intended for the diagnosis, prevention or treatment of a serious or chronically debilitating pathology that affects up to 5 in 10,000 people in the European Union. This status is attributed to the medicine when it is authorised to be placed on the market, and is normally withdrawn after 10 years. **Clinical and epidemiological information** ▪ With the aim of contributing to the design of the national registry of rare diseases, a meeting was held on 27 March 2017 at INSA, with more than 25 participants, including participants from the following entities: Reference Centres (9), DGS (1), ACSS (2), INSA (8),

	INFARMED (1), SPMS (2), patient associations (1), scientific society (1), among others. In dialogue with the different interest groups, a consensus was reached that it would be appropriate to start by establishing a registry of rare pathologies (or groups of pathologies) for which Reference Centres have been, or are in the process of being, established, namely, hereditary metabolic diseases (including lysosomal overload diseases), paramyloidosis, rare paediatric cancers, cystic fibrosis and congenital coagulopathies. As a structure for data collection (directly from the electronic clinical process without double entry) the minimum data set recommended by the European Union's EPIRARE initiative (2014) was proposed. ▪ Taking as a reference the voluntary registration of rare diseases, associated with the issuance of the Rare Disease Person Card, it appears that around 52% of the cards issued are carried out by ARS Norte units, 26% by ARS Lisboa and Vale do Tejo, 20% from ARS Centro and 2% from ARS Algarve. The diseases with more than 100 cards issued are Cystic Fibrosis, Familial Amyloidotic Polyneuropathy, Haemophilia A and Phenylketonuria. ▪ The activity planned to improve the level of training of professionals linked to the area of education, who support people with rare diseases, aimed at the entire educational community on special health needs, which was expected to be implemented through a national seminar was replaced by local sessions, in school groups, for awareness raising and training. **Research** ▪ In this context, INSA and FCT organised an international scientific meeting on modern research trends in rare diseases, "Rare Disease Symposium 2017: From research, a world of possibilities", on 15 December 2017, in Lisbon, broadcast by video conference at INSA Porto facilities. One hundred and seventy people participated in this meeting. One of the practical results of this initiative is the elaboration and validation of Research and Development agendas (still ongoing) aiming to improve knowledge about (i) mapping and diagnosis of rare diseases, (ii) models, mechanisms and development of therapeutics and (iii) resources for those (living) with rare diseases. A survey was also made of projects financed in Portugal in the last five years with a focus on rare diseases. **Social integration and citizenship** ▪ The Commission planned, for 2017, to help civil society organizations that provide support to people with rare diseases and their families to design their proposals to apply for external funding. There were no eligible contests.
Governance and organisational structures	*See Integrated Strategy for Rare Diseases 2015-2020 and Annual Plan 2017.*
Funding model	Some initiatives were not fully implemented due to local constraints related to: ▪ Budget cuts made at the beginning of 2017 in the order of 30%, in some partner institutions. ▪ Lack of specific budget allocated to the activities of the Integrated Strategy for Rare Diseases 2015-2020. ▪ Impossibility for the entities involved to accept external financing from private, for-profit entities. In view of the above, activities for 2018 will have to be programmed within the strict domain of skills and resources available from the different partners of the Strategy, with possible limitations in the definition of some objectives.
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	*See 'Access to early diagnosis'.*

Personalised medicine, genomics, genetic counselling	*See 'Access to early diagnosis'.*
Models of care/care pathways	*See 'Coordination of care', 'Access to early diagnosis' and 'Access to treatment'.*
Workforce	*See 'Clinical and epidemiological information' (seminar).*
European Reference Networks	*See Coordination of care', 'Access to treatment' and 'Clinical and epidemiological information' for references to Reference Centres.*
EU alignment and participation	*See 'Access to treatment (Update of the Orphanet portal) and Clinical and epidemiological information' (EPIRARE minimum data set).*
Health information (including rare disease registries)	*See 'Coordination of care' (Rare Disease Person Card), 'Clinical and epidemiological information' (national registry).*
Orphan medicines	*See 'Access to treatment' (Update of the Orphanet portal).*
Rare disease research	*See 'Research'.*
Alignment beyond the healthcare sector	*See 'Coordination of care' (satisfaction survey) and 'Social integration and citizenship'.*
Any additional information (for example, background to the strategy or strategy development)	*N/A.*

Key: RDPC: Rare Diseases Person Card; INSA: National Institute of Health Dr. Ricardo Jorge; FCT: Foundation for Science and Technology.
Note: The information in this table was extracted from a version of the original document translated to English using Google Translate.

Table B28. Data extracted for Scotland (Rare Disease Action Plan).

Scotland	Strategy information
Author(s) **Title**	Scottish Government Rare Disease Action Plan[42]
Timeline	2022-2025, approximately **Timescales for action** The [UK] Rare Disease Framework has a lifespan of five years, and as we have learned from previous strategies, actions set out in year one can quickly expire or change due to innovation or the evolvement of other policies that replace the original action. With that in mind, this document sets out the specifics of our short term to medium term actions (2–3 years) and our ambitions for the long term (3+ years). Over the course of the next five years, we hope to have many iterations of this Action Plan building our medium-and long-term ambitions into actions.
Overall aim(s)	This Action Plan, and the further iterations that will follow, will set out the measures the Scottish Government will take to put into action the priorities of the UK Rare Diseases Framework. We will achieve this by working with partners across NHS Scotland, third sector organisations and beyond, and continue to strive to ensure that all people living with a rare disease are able to access the best possible care and support.
Themes and or priorities	4 priorities the same as the UK Framework: **Priority 1: Ensuring patients get the right diagnosis faster** **Priority 2: Increasing awareness of rare diseases among healthcare professionals** **Priority 3: Better coordination of care** **Priority 4: Improving access to specialist care, treatment and drugs (Actions 15-18)** **Priority 1: Ensuring patients get the right diagnosis faster (Actions 1-3 below)** Our vision is for people living with a rare disease across the UK to get a final diagnosis faster and for research into previously unrecognised conditions to identify new rare diseases and provide new diagnoses. *What Matters to You?* [*a snapshot of the feedback we have received from the rare disease community*] ▪ Identify new rare diseases and ways to diagnose them ▪ Having access to genetic testing ▪ Faster patient diagnosis ▪ Healthcare professionals to 'think rare' when presenting with symptoms ▪ Expanding newborn screening for conditions such as Spinal Muscular Atrophy (SMA) ▪ Accelerated adoption of new diagnostic interventions ▪ Embedding counselling and mental health support as part of the diagnostic journey **Priority 2: Increasing awareness of rare diseases among healthcare professionals (Actions 4-8)** Our vision is for healthcare professionals to have an increased awareness of rare diseases and use of genomic testing and digital tools to support quicker diagnosis and better patient care. *What Matters to You?*

	▪ Healthcare professionals to have better, easier access to information about rare conditions ▪ Be aware of issues of diversity, such as ethnicity, and respect individual characteristics ▪ Be aware of how to manage transition from paediatric to adult services ▪ Raise the profile and visibility of rare conditions ▪ Embed rare conditions in training ▪ Increase awareness among medical professionals ▪ Raising the general public's awareness of rare diseases and their effects **Priority 3: Better coordination of care (Actions 9-14)** Our vision is for people living with a rare disease to experience better coordination of care throughout the patient journey. *What Matters to You?* ▪ Take the 'whole picture' of my condition into account when seeing different specialists ▪ Consensus documents and co-produced care plans ▪ Alert cards and patient passports ▪ The opportunity for a proper discussion about my priorities for my care ▪ Better co-operation in sharing data across record systems ▪ Better patient assessment when seeing specialists ▪ Make Mental Health support available at all stages of patient journey **Priority 4: Improving access to specialist care, treatment and drugs (Actions 15-18)** Our vision is for people living with a rare disease to have improved access to specialist care, treatments and drugs. *What Matters to You?* ▪ Enable access to specialist centres across the UK ▪ Choice between telecare and face-to-face as preferred ▪ Ensure the Highlands and Islands aren't 'left behind' ▪ Develop new drugs for rare disease and make them accessible ▪ Enable participation in rare disease research and share more information about it ▪ Ensure a nationwide approach is taken across Scotland ▪ More methods of communication with medical professionals and specialists **Annex – Underpinning Themes** ▪ **Patient Voice** People living with a rare disease are best placed to shape and influence our policies on rare diseases. We recognise this and have embedded the voice of those living with a rare disease into the government of our Action Plan. However we also recognise the need to identify the best method of engagement to ensure it doesn't add a burden on to patients and carers. We will work with rare disease organisations to achieve this, taking advantage of existing groups and platforms wherever possible. ▪ **National and international collaboration** The small numbers of patients with individual rare diseases make collaboration essential, both for the support of patient care and the delivery of robust research. We are committed to continuing collaboration with the rare disease community across the world, including patients, healthcare professionals, researchers, and industry, to share knowledge and ideas to improve outcomes.

	We will continue to work closely with our counterparts in the UK Government and the other devolved administrations to ensure close alignment of the rare diseases Action Plans that each of the four nations has developed. One key area of collaboration is on national registries for congenital anomalies. ▪ **Pioneering research** Participation in research, and promotion of opportunities for research, play vital roles in how our healthcare is delivered and improved. We have set out a clear action in this plan on how we might address this. This is at the centre of all we do. For people living with a rare disease, research can fulfil unanswered questions that may support a diagnosis, cause, symptoms and treatment for many rare diseases. The Scottish Government, through the Chief Scientist Office (CSO), has established and maintained an active programme of co-funded research with third sector organisations, including research in rare diseases. NHS Research Scotland is committed to actively involving patients, those who care for them and the public in all aspects of the research process. This includes shaping future research activity and there are currently supporting more than thirty genetics studies, about a third of which are led from Scotland. We will continue to work with CSO and the NHS Research Scotland infrastructure to enable more opportunities for people with rare genetic diseases to participate in research, which in turn leads to improved care and the development of new treatments. ▪ **Digital, data and technology** Across health and social care, we are using data more efficiently and effectively than ever before, empowering patients to take better control of their health and care journey. The Covid-19 pandemic has increased our reliance on digital developments and accessible data, and we want to harness these advances to create a more seamless digital experience in healthcare moving forwards. As referenced earlier in the plan, the Digital Health and Social Care Plan and subsequent delivery plan will be central to this underpinning theme. While not specific to rare diseases, the Digital Health and Social Care Plan sets out a number of actions which will benefit people living with a rare disease by improving access to care, reducing the burden of coordinating their care and improving access to the information they need to live their lives. ▪ **Wider policy alignment** We recognise that the impact of living with a rare disease is much wider than just a person's health. Due to the nature of their condition, many people living with a rare disease require housing adjustments, social care, financial aid, mental health support and special educational needs support. Wider policy development in these areas must reflect the needs of those with rare conditions. Over the long term (3+ years) and linked with our patient voice priority we will work with policy makers across Scottish Government to put forward the needs of the rare disease community when developing policy. Given the importance of genomics in improving diagnosis for some rare diseases, and to support new research into potential treatments, our plans will align with our Genomics Implementation Plan, as well as other relevant strategies and policies. We will work with policies across the Scottish Government to ensure those living with a rare disease are represented during the development of relevant policies.
Targets (if specified) and measurement method(s) (where available)	**Priority 1…** **Monitoring and Evaluation** We recognise that measuring outcomes for patients, carers and families will be difficult. However, measuring the success of our actions in the short to medium term will be achieved in different ways, depending on what needs to be measured. Work such as better signposting of awareness-raising resources can be measured by assessing their take-up among healthcare professionals, and professional and patient reported improvements in the time taken to diagnose. We will look to develop metrics by which to measure the success of our various actions, such as patient-reported outcome measures.

Implementation action(s), lead(s) and key performance indicator(s)	**Action 1: Implementation of Genome UK** Back in September 2020, the Scottish Government signalled support for Genome UK (published that month). This strategy sets out how the genomics community will work together to harness the latest advances in genetic and genomic science, research, and technology for the benefit of patients. This community includes patients, families, charities and officials across the four nations, NHS bodies, academia, and industry amongst others. With all four nations signalling support for the strategy, this provides a blueprint for expanding our genomics offering across the UK. Since the publication of Genome UK, the four nations have worked closely to develop a series of shared commitments: Genome UK: Shared Commitments for UK-wide implementation 2022 to 2025 (March 2022). This publication signals a commitment to work together with our delivery partners across the UK in order to realise the potential of genomic technologies for the benefit of patients at home and abroad, including supporting people living with a rare disease. ▪ In Scotland specifically, we have recently established the Scottish Strategic Network for Genomic Medicine, as a 'front door' for engagement and strategy development. The Network will advise and make recommendations on genetic testing availability as well as supporting the planning for future capacity into areas such as Whole Genome Sequencing or expanding our Whole Exome Sequencing services, which we recognise are of huge importance to the rare disease community. The Network will have a crucial horizon-scanning function which will work with the Scottish Medicines Consortium, Scottish Health Technology Group, researchers, academia and our Innovation Pipeline to ensure people with a rare disease can access new genomic technologies and testing. ▪ Soon after the publication of this Action Plan, we will publish our first ever genomics publication, which will set out our intention for developing Scotland's genomics medicine services over the next five years. This will be following by Scotland's first ever genomics strategy in the course of 2023, which will build on work to date, including the Bridge to a Scottish Genomics Strategy, which focused on rare disease genomics, but also explore how we further propel our genomics offering, benefitting those who need it most. Most importantly, our strategy will have a real focus on rare and inherited conditions with the support of the appointed Network Clinical Lead for Rare Disease, Dr Jonathan Berg. The Scottish Government will support this strategy through significant investment, with £5 million committed for 2022/23 alone, previous investment of £8 million since 2017. This is in addition to almost £20 million of funding allocated to the four genetic laboratories annually in Scotland by NHS Boards through NHS National Services Division (NSD) commissioning arrangements. ▪ We also recognise that we must have capacity within our genetic laboratories to deliver an equitable service for rare disease patients. For this reason, we will be implementing the recommendations from the Major Service Review of Scottish Genetic Laboratories. By acting on these recommendations, we will ensure that our genetic medicine service is fit for the future and can flex to meet increasing demand and advances in the field to benefit a range of conditions, covering both cancer and rare diseases. ***Action 1: What does this mean for people living with a rare disease?*** The needs of those with a rare disease will be a key consideration on how we expand our genomic medicine services in Scotland. The Rare Disease Implementation Board for Scotland will work closely with the new structures, becoming advocates for the rare disease community. In addition, we will ensure relevant rare disease clinicians and patients' representatives can feed directly into our implementation plan by being part of the new structures. The rare disease clinical lead for the Genomics Network will be key to this. **Action 2: Newborn Screening** Screening has a vital role in allowing early diagnosis of some rare diseases and the initiation of early treatment to reduce complications. The Scottish Government is represented on the UK National Screening Committee (UK NSC) which makes its recommendations to all four Health Departments across the UK.

	The UK NSC advises Ministers and the Health Service in all four UK nations on all aspects of screening. Using research evidence, pilot programmes and economic evaluation, the Committee assesses the evidence for national screening programmes against a set of internationally recognised criteria, taking a range of distinct factors into account. At present, nine rare conditions are screened in newborn babies through the NHS Newborn Blood Spot Screening Programme. The UK NSC has recently undergone significant changes to both its remit and membership and will now consider recommendations for targeted as well as national screening programmes. ▪ For our year one action, we commit to continuing to participate in the UK NSC; to following guidance to ensure appropriate use of screening tools in line with UK National Screening Committee recommendation, and to work with the Committee to embed its new remit. ▪ Through the Rare Disease Implementation Group, we will engage in any considerations on newborn screening, ensuring the voice of those with a rare disease are part of any future screening considerations. ▪ We will also continue to engage across the four nations on any new UK-wide screening research pilots. ▪ Furthermore, we will consider Scotland's participation in the UK National Newborn Screening Pilot which aims to carefully evaluate the benefits and risks of implementing newborn genomic screening to accelerate diagnosis and enable earlier access to treatments for rare genetic conditions. ▪ In addition to this, through our engagement with the rare disease community, we realise the need to improve the understanding of screening policies particularly for rare diseases. Over the next 12 months, we will work with the rare disease community to improve the understanding of screening decision-making processes. We will look to embed this information into existing materials, ensuring it is readily available and understandable by those impacted by such policies. ***Action 2: What does this mean for people living with a rare disease?*** Those living with a rare disease will have access to key information on screening in Scotland. In particular, we will equip the rare disease community with information on how screening policies are agreed and the processes on expanding screening programmes. Information will be made available to those living with a rare disease, so that so they understand how screening impacts on them and their families. **Action 3: Expanding the functionality of the Congenital Conditions and Rare Diseases Registration and Information Service for Scotland (CARDRISS).** Congenital conditions are important in their own right, and also comprise a key subgroup of all rare diseases. Initial funding to establish CARDRISS was provided by the Scottish Government to NHS NSS Information Services Division (ISD) and latterly to Public Health Scotland (PHS), the current home of CARDRISS, over the three-year period October 2018 to March 2022. ▪ In the first instance, CARDRISS will register babies affected by a major structural or chromosomal anomaly or recognised syndrome. This is in line with the standards recommended by the European Registry of Congenital Anomalies and Twins (EUROCAT), a European network of congenital anomalies registers. Live-born babies diagnosed within the first year of life; spontaneous stillbirths occurring at ≥24 weeks gestation; spontaneous late foetal losses occurring at 20–23 weeks gestation, and pregnancies terminated at any gestation due to an included anomaly will all be registered. ▪ In due course, when registration of major anomalies is securely established, the plan will then be to widen the remit of CARDRISS to include registration of other rare diseases. This will help inform the planning of services for individuals and families affected by congenital anomalies and rare diseases. It will also allow NHS Scotland to support the prevention of anomalies where possible, understand the impact of antenatal screening and support research into these conditions. ▪ At the beginning of the project the plan had been that CARDRISS would prospectively register affected pregnancies, ending in 2021 onwards. Work on the CARDRISS IT system then took longer than expected, due to the Covid-19 pandemic. The registration of affected pregnancies was therefore delayed until the summer of 2022. In recognition of the quality of the linked database, Scotland has been

accepted as an associate member of the European network of population-based registries for the epidemiological surveillance of congenital anomalies (EUROCAT). A data-sharing agreement with EUROCAT is in place, and aggregate data covering pregnancies ending 2005-2019 will be transferred to the central European database on congenital conditions for publication on the EUROCAT website, inclusion in country level-monitoring of trends and clusters of conditions, and in international studies.

- Over the medium term, we will work with PHS to build on the success of CARDRISS and explore how the functionality of the CARDRISS IT system can further support data capture for rare diseases. This will include exploring options for establishing new national data returns. New national data returns would also bring wider benefits, in particular supporting monitoring of the pregnancy and newborn screening programmes. PHS will also explore how the registration of babies can be extended to focus on rare diseases covered by the pregnancy and newborn screening programme. Specifically, this could include the inherited metabolic disorders (IMDs) currently covered by the newborn screening programme.
- We will work with PHS to understand the options to expand CARDRISS. Extensions are likely to require financial investment by the Scottish Government, which we will consider as part of our future budgetary considerations.

This action is linked to action 18.

Action 3: What does this mean for people living with a rare disease?

Having access to better data on rare disease can help clinicians make better informed decision on care, prevent disease and also allow better access to research and clinical trials. While those living with a rare disease won't necessarily have access to CARDRISS, they will see benefit through their care as well as support for future diagnoses.

Action 4: Improving information about Rare Disease on NHS Scotland platforms

The importance of having access to accurate and timely information has been clearly seen and highly valued by us all in the last two years. A key platform for hosting NHS information in Scotland is NHS Inform. NHS Inform has been at the forefront of providing crucial information to people across Scotland throughout the Covid-19 pandemic. It has become the first point of call for many seeking advice and information relating to health services.

- Over the next 12–18 months we will work with NHS Inform to improve information about rare diseases online. We recognise that due to the volume of rare diseases we will be unable to have bespoke information for each rare disease. However, as part of their patient journey, we want to ensure people have access to relevant information and are signposted to places for support while living with a rare disease or waiting to receive a diagnosis of their condition.
- In doing so, we will work with third sector organisations to develop supporting materials which for hosting via NHS Inform. We will look to use existing work such as the Genetic Alliance UK Rare Resources for Scotland Toolkit, but we will also work with our Patient Voices Advisory Group to further understand what information they would expect to see on a national platform about rare diseases.
- Furthermore, we will seek further opportunities to improve the information about rare diseases on NHS Scotland digital platforms, including those used by healthcare professionals themselves.

Action 4: What does this mean for people living with a rare disease?

Those newly diagnosed with a rare disease will be able to seek initial information on NHS Inform, and signposting towards further resources. This could be the difference between a person dealing with their diagnosis alone or accessing support groups and information which we know are crucial to individuals. The information may also highlight additional support spaces that those already living with a rare disease may not have been aware of.

Action 5: Optimising Rare Disease Day

	Rare Disease Day is an internationally recognised day. On the last day of February every year the rare disease community comes together to raise awareness of rare diseases and their impact. The day is an opportunity to truly maximise our awareness-raising powers for rare diseases. In the past, the Scottish Government has supported Rare Disease Day through Parliamentary events, lighting up buildings in homage to the day as well as publishing an open letter to the rare disease community. ▪ Rare disease day provides an important platform to raise awareness of rare diseases, and we will seek to optimise this platform to support the delivery of this priority. We will work with stakeholders to develop a suite of events which engage a broad range of people including clinicians, senior leadership in NHS Boards and those working within primary care. We recognise that raising awareness is about reaching those who aren't already engaged or have not yet gained some awareness of rare diseases. Those are who we will target through this action. ***Action 5: What does this mean for people living with a rare disease?*** Using the internationally recognised Rare Disease Day can provide more opportunities provide more opportunities to raise awareness of rare disease. We want to ensure we take full advantage of this so that raising awareness continues to move forward. **Action 6: Working with NHS Education for Scotland** NHS Education for Scotland (NES) is the national health board with statutory responsibilities to effect sustainable change through workforce development, education and training across the health and social care system in Scotland, while working at UK level with partner organisations. NES's purpose is to drive change and improve the quality of care experienced by citizens across Scotland by ensuring that the health and social care system has the right staff, with the right skills, in the right place, at the right time. NES is integral to improving outcomes for people and in ensuring a skilled and capable workforce underpins the design and delivery of services. NES will be a key partner in our efforts to increase awareness of rare diseases among healthcare professionals and over the course of this plan we will establish partnership working to enable this. ▪ Over the next 12 months, we will work with NES to understand the existing rare disease training and education material already developed by a range of organisations like those developed by Genetic Alliance UK, Medics 4 Rare Disease and in other nations. We will consider where these training and education materials can be hosted to ensure optimal recognition and pick up across Health Care Professionals. ▪ One key platform is Turas. Turas is a modern and accessible digital platform developed by NHS Education for Scotland to support health and care professionals working in the public sector. We will work with NES and in partnership with these third sector organisations to understand how we utilise national platforms like Turas to continually raise awareness of rare diseases. ▪ We know the importance of linking training with Continuing Professional Development (CPD) points. Linking rare disease training with CPD points will ensure maximum uptake by healthcare professionals, and over the medium term (2–3 years) we will explore the appetite for this and how to enable it. ▪ Over the longer term (3–5 years), we will seek to work with NES and a range of other educational partners to consider how we embed basic training on rare diseases into the curriculum for undergraduate and post-graduate students. This will be challenging, but we recognise that to significantly improve awareness of rare diseases it is imperative that we do so as early as possible in the education pathway for healthcare professionals, particularly in nursing and GP training. Exploring where links can be established in existing curricula will be a useful starting point in such considerations. ***Action 6: What does this mean for people living with a rare disease?*** Healthcare professionals having access to key information on rare disease will support the full patient journey. Importantly, building in rare disease training and education to the curriculum for healthcare professionals will ensure that those who work on our frontline services can do so with a basic understanding and awareness of rare disease.

	Action 7: Enabling opportunities for third sector organisations to raise awareness of rare diseases We recognise the crucial role that organisations like Genetic Alliance UK, the Office for Rare Conditions and Medics 4 Rare Diseases play in increasing awareness of rare diseases. ▪ Through partnership working, we will seek to work with rare disease organisations to enable opportunities for awareness raising. We will facilitate introductions and connections wherever possible between these organisations and their valuable expertise and NHS Scotland bodies like NES and NHS Inform to ensure that their work can reach the widest audience. ▪ We will seek to utilise existing platforms such as NHS Scotland events and conferences as well as facilitating opportunities to bring rare disease awareness raising to the door of primary care, hospitals and community settings. ▪ We recognise that the power in awareness raising lies in amplifying the voices of those most affected. We will therefore ensure that any opportunities to engage with healthcare professionals include the voices of the rare disease community. Sharing the lived experience of rare diseases with those working with patients on a daily basis will have the most powerful impact. ▪ Through working with charities and other third sector organisations we will look to better understand the needs of healthcare professionals when it comes to rare disease. It is important that we are providing materials and information which are of use to healthcare professionals. ▪ We will also look to work with Medics 4 Rare Diseases in a useful piece of work to assess the current levels of rare disease awareness and understanding among medical students. From the results of this survey, we will be able to see where there are gaps and what further action we should be taking to address them. ***Action 7: What does this mean for people living with a rare disease?*** We recognise we can't deliver this plan alone. Working with organisations who have direct links to the rare disease community will be crucial to the success of this plan. By doing so, we will be able to strengthen our engagement and make more progress which will ultimately have a positive impact for those with a rare disease. **Action 8: Understanding and acting on the information needs of Health Care Professionals to raise awareness of rare diseases** To further our understanding of what healthcare professionals need to improve their awareness of rare diseases, we will work with Genetic Alliance UK and the Office for Rare Conditions. ▪ Genetic Alliance UK's research team will develop a survey to understand healthcare professional's views of rare conditions, assess level of awareness and to identify gaps in information needs and how to address them. This will be distributed through Genetic Alliance UK's communications team, Office for Rare Conditions communications team and wider NHS Scotland networks. This will inform the development and distribution of information materials. ▪ Following the results of the survey Genetic Alliance UK and the Office for Rare Conditions will re-develop the Rare Resources Professionals Guide, which focuses on signposting healthcare professionals to reliable sources of information, to ensure it meets the needs of healthcare professionals in Scotland. We will also develop promotional materials such as posters and business cards for distribution in appropriate healthcare settings. ▪ Furthermore, we will work with Genetic Alliance UK and the Office for Rare Conditions to support the development of a programme of events and activities to coincide with Rare Disease Day 2023 to improve awareness of rare conditions with NHS Scotland staff. ***Action 8: What does this means for people living with a rare disease?***

	Having more tailored resources available to medical students and healthcare professionals will help to raise the profile of rare diseases and empower them to 'think rare'. Getting the awareness raising priority right means that all the others will follow – diagnostic odysseys will be reduced, and people living with rare diseases will have better and quicker access to the treatment and care that care that they require. **Action 9: Consider a future Care Coordination Service** Identifying a suitable coordination of care model for use in Scotland is a process that we have already started to consider. We also began from the recommendation in the Framework that coordination of care should be improved, and also had recent reports to consider: ▪ The Scottish Parliament Cross Party Group on Rare, Genetic and Undiagnosed Conditions, via Genetic Alliance UK (the CPG secretariat) published the report Improving Care for Rare Conditions in Scotland in March 2021. The report recommended that a short-life group should be established to explore a coordination of care model for Scotland, and that the Scottish Government should commit to a pilot project for a care coordination service. ▪ The COordiNated Care of Rare Diseases (CONCORD) study began in 2018 and was published in March 2022. This UK-wide study found that poorly coordinated care can be detrimental to patients and families, and suggested classifications and flowcharts for effective care coordination. We have also heard from our programme of patient engagement that people living with rare diseases often end up coordinating their own care (or their child's care), as there can be so many specialists and appointments to deal with and organisational coordination is lacking. This takes up lots of time, money and energy and can become a full-time role. We stood up a Care Coordination Working Group in 2021 as part of our Rare Disease Implementation Board. The group began by looking at models of good practice and considering how one of these might be adopted or adapted for use in Scotland. This information-gathering exercise provided useful insights into care coordination models that have been successfully implemented. One such model is the East of Scotland Clinical Genetic Service that has been developed in NHS Tayside. ▪ We will use the information gathered, such as the example above, as a starting point to consider a future care coordination service for people living with rare diseases in Scotland. This will include looking at the role of genetic nurses in supporting coordination of care and considering whether we can develop a model for Scotland. ▪ Getting the right model for Scotland will take time and is likely to need investment, but this is worth implementing in the right way so that those who need coordinated care can benefit from joined-up expertise. We will continue to prioritise this area and take advantage of the expertise available in our stakeholder networks. ***Action 9: What does this mean for people living with a rare disease?*** Having a suitable model of care coordination implemented in Scotland will mean that people living with rare diseases will have fewer wasted appointments, benefit from the expertise of multi-disciplinary care, experience shorter diagnostic odysseys, and ultimately benefit from care that is better tailored to their needs. **Action 10: Improving the use of Anticipatory Care Plans** Anticipatory Care Planning is a person-centred, pro-active approach to care that involves conversations between individuals, their families, carers and health and social care professionals. It helps people communicate goals and preferences for their care. Anticipatory Care Plans, or ACPs, are the way these conversations are recorded. They can be updated as required, for example if a person's condition changes, or if they develop additional needs. ACPs are sometimes associated with end-of-life care, but in this context, they are about living with a long-term condition and communicating what is important to the person who lives with that condition. Information about Anticipatory Care Planning and ACPs is hosted on Healthcare Improvement Scotland's "iHub" website. There is also information on Anticipatory Care Planning

being used in the context of Covid-19, or for neurological conditions. ACPs can contain valuable information about the complexities of living with a rare disease. For example, if emergency care were required, and a person's condition meant that they had specific needs, allergies or could not be intubated, an ACP can make this clear to the responding medics. We know that there are useful information resources relating to Anticipatory Care Planning and the use of ACPs, such as the aforementioned pages hosted by Healthcare Improvement Scotland.

- We want to encourage take-up of ACPs among healthcare professionals and signpost this information to clinicians and teams who care for people living with rare diseases.
- Over the next 12–18 months, we will work with Healthcare Improvement Scotland and third sector organisations on ACP information and resources that relate to rare diseases, along the same lines as those for neurological conditions. We will look for opportunities to promote the use of Anticipatory Care Planning when we are considering the training and education aspects of our Action Plan. We will then publish updates on progress in this area.

Action 10: What does this mean for people living with a rare disease?

The use of Anticipatory Care Planning by people living with a rare disease or condition can lead to better coordination of care. When "what matters to you" has been discussed and clearly noted on an ACP, it can be used by all the healthcare professionals involved in a person's care and treatment. The goals and wishes identified by the person living with the rare condition can be considered by multi-disciplinary teams when they are planning the right levels of care for that person.

Action 11: Digital Passports

Patient passports have been around for some time, and were in use in Scotland in the 1990s, first in paper form and then as digital documents, this development supported by the Scottish Government. A digital patient passport is a simple to use document in the style of an e-book, which can hold information about a person's needs, priorities for their care and their life and family. Similar to the way ACPs can be used, patient passports enable a person living with a long-term condition to record what matters to them. The ACP can then be shared among multiple healthcare professionals and specialisms to ensure they all have access to the same information. This is another way to improve care coordination.

- To explore how this could benefit people living with a rare disease, we will work with third sector organisations who have used patient passports to understand how they could be better promoted for use by people living with rare diseases, their families and healthcare professionals.

Action 11: What does this mean for people living with a rare disease?

The wider availability and adoption of care passports will provide another way for people living with a rare disease to inform healthcare professionals of their priorities for their care. If different healthcare specialities all have access to this same information, patients won't have to spend as much time explaining the same things at appointments. More appointment time is then freed up for discussing current needs and priorities.

Action 12: Supporting the Implementation of: It's OK to Ask

In 2021, NHS Scotland launched the public campaign "It's OK to Ask". Developed and piloted by NHS24, and support by the Scottish Government's Realistic Medicine Value Improvement Fund, the campaign encourages people to ask healthcare professionals four key questions:

- What are the benefits of my treatment?
- What are the risks of my treatment?
- Are there any alternative treatments I can try?
- What if I do nothing?

	The campaign states that knowing the right questions to ask at healthcare appointments can make all the difference. This enables people to make the right decisions about their treatment and care. The webpage includes a downloadable patient leaflet that can be taken to appointments. ▪ We would like to encourage the take-up of "It's OK to Ask" as widely as possible. Wider adoption of "It's OK to Ask" would also assist healthcare professionals in knowing a person's wishes and priorities, leading to more productive discussions at appointments. Transitions from paediatric to adult care can also benefit from this approach. ***Action 12: What does this mean for people living with a rare disease?*** We know that people living with rare diseases, or the parents of children with rare diseases, will already come to appointments with a high level of knowledge about their condition (once it has been diagnosed). This could still be a helpful method of focusing appointment time so that people living with a rare disease are able to get the most out of every appointment and have more control over their priorities for their care. **Action 13: Mental Health Strategy** Our programme of rare disease community engagement has highlighted that people living with rare diseases place a high priority on mental health: improving resources, more tailored support and generally reducing the burden that living with a rare disease can have on their mental health. Mental health services can be required at any stage of the patient journey, from the diagnostic odyssey and the processing of a diagnosis, to ongoing support when accessing care and treatment. The Scottish Government's Mental Health Strategy 2017–2027 was published on 30 March 2017. The Strategy set out actions to be achieved with the guiding ambition that we must prevent and treat mental health problems with the same commitment, passion and drive as we do physical health problems. The Scottish Government committed to reviewing and refreshing the Mental Health Strategy in 2022. ▪ As part of our considerations for a future strategy, we will consider the mental health needs of all patient groups, including people living with rare diseases. Throughout the development we will work to ensure that we reflect the voice of those living with a rare disease in the refreshed strategy. ▪ We will also look to work with Genetic Alliance UK and other organisations to consider developing downloadable Mental Health resources for those living with a rare condition. ***Action 13: What does this mean for people living with a rare disease?*** Considering the needs of people living with rare diseases when developing mental health policy and resources means that tailored resources can be developed. Promoting these more widely will mean that people's mental health needs can be integrated into their care. **Action 14: Continuing to Promote and Embed Person Centred Care** Practical improvements to person-centered care are promoted and supported through a framework of five key "Must Do With Me" principles: 1. "What matters to you?" Your personal goals and the things that are important to you have been discussed and form the basis of your care or treatment. 2. "Who matters to you?" We have asked you about the people that matter most in your life and we have given you the opportunity to involve them in the way that you choose. 3. "What information do you need?" We have provided you with understandable full information and supported you to make decisions that take account of your personal goals and the things that are important to you.

	4. "Nothing about me without me." You will always be given the opportunity to be involved in discussions. All information exchanges and communication between professionals or between different services or supports are transparent and always provide you with the opportunity either to be present or to contribute to the process. 5. "Personalised contact." As much as possible, the timing and methods by which you contact and use services or supports are flexible and can be adapted to your personal needs. Together, these five "Must Do With Me" areas will help to ensure that all the interactions between people using services and the staff delivering them are characterized by listening, dignity, compassion, and respect. ▪ We will continue throughout the lifespan of this person-centred framework to promote and embed person centred care ensuring those with lived experience are at the heart of the services we are delivering. ▪ We will continue to take a "what matters to you" approach to our engagement. We recognise the need to continue our engagement with the rare disease community from development through to implementation of our Action Plan. ***Action 14: What does this mean for people living with a rare disease?*** These five principles, once embedded in regular practice at appointments, will help people living with rare diseases to get the most out of every consultation, and have their wishes and priorities at the centre of the conversation. **Action 15: Recognising the role of specialist services** Specialist services and national networks are commissioned through National Commissioning by NHS National Services Scotland on behalf of NHS Boards and the Scottish Government, to provide quality assurance for a range of specialist interventions for people living with rare diseases. These national commissions help ensure patients across Scotland have the best possible access to high quality specialist care. NSS brings together a diverse team of programme management and commissioning experts including clinical and public health, all working within the governance of NHS Scotland. This team works working with a service provider to set a service specification, agree the activity profile, staffing, and resources required to commission a service that demonstrates positive clinical outcomes and patient experience. These commissioned services are critical to coordination of care. NHS National Services Scotland will continue to support the development of services for rare diseases where possible, and engage with the clinical and rare disease community to ensure they are fully involved in service planning. ▪ We recognise too that there are a wide variety of non-commissioned specialist services across Scotland, covering a range of rare conditions. These clinics or specialists are not always evident, and we will work to understand the landscape of care pathways across health and social care in Scotland, by initially focusing on an agreed set of rare conditions. ▪ We will seek to understand the availability of clinics for these non-commissioned conditions and increase the awareness of these specialist services to ensure patients have appropriate access. It is important to highlight that referral out with a patient's host NHS Board is at the discretion of the host and receiving Boards. ***Action 15: What does this mean for people living with a rare disease?*** If we ensure that we consider the needs of people living with rare diseases when planning future services, people who need these services will have a clear pathway for referral and treatment when clinically appropriate. This will improve access to the right care at the right time. **Action 16: Ultra Orphan Pathway** The Scottish Government recognises that for people living with ultra-orphan diseases (those affecting fewer than 1 in 50,000 people), there tends to be no or a very limited number of medicines available to treat their specific condition. Ultra-orphan medicines often face difficulties being approved through traditional health technology assessments, due to the low number of patients available to take part in clinical trials, and thus there can be higher uncertainty about their efficacy and cost effectiveness. The 2016 Montgomery Review of Access to New

	Medicines highlighted that there was a need to accelerate access and provide advice on medicines for ultra-orphan diseases. In Scotland, the Scottish Medicines Consortium (SMC) appraises the clinical and cost-effectiveness of newly-licensed medicines. The SMC carries out appraisals of new medicines, based on the clinical and cost-effectiveness of the medicine at a population level. The SMC then determines whether a medicine should be accepted for routine use within the NHS in Scotland, and publishes advice for Health Boards. The 2016 Montgomery Review recommended that an alternative assessment pathway be developed for ultra-orphan medicines that preserves the integrity of the SMC and its processes, yet achieves a level of access to these medicines that is comparable for orphan and end-of-life medicines. In response to the review findings, the Ultra-Orphan Pathway was launched in 2018, to support people living with ultra-orphan diseases to receive faster access to new and innovative medicines. The Ultra-Orphan Pathway supports pharmaceutical companies to make medicines available through the NHS in Scotland for an initial period of three years, to enable further data collection on the medicine's efficacy, prior to a further review by the SMC on its routine use in NHS Scotland at the end of the initial three year period on the pathway. Since 2018, a number of medicines for rare diseases have become available through the Ultra-Orphan Pathway, such as nusinersen (Spinraza®) for the treatment of 5q spinal muscular atrophy, and burosumab (Crysvita®) for the treatment of X-linked hypophosphatemia in children and adolescents. The introduction of the Ultra-Orphan Pathway has and continues to support patients to receive faster access to new medicines for rare diseases. ***Action 16: What does this mean for people living with a rare disease?*** By taking on board feedback from the rare disease community and from healthcare professionals, we will ensure that our engagement with new medicines takes account of the community's priorities. Better access to new medicines will improve treatment and care for people who can benefit from these developments. **Action 17: Digital Front Door** This action impacts several priorities. We are using data across health and social care more efficiently and effectively than ever before, empowering patients to take better control of their health and care journey. The Covid-19 pandemic has increased our reliance on digital developments and accessible data, and we want to harness these advances to create a more seamless digital experience in healthcare for the future. As referenced earlier, the Digital Health and Social Care Plan and subsequent delivery plan will be central to this underpinning theme. While not specific to rare diseases, the Digital Health and Social Care Plan sets out a number of actions which will benefit people living with a rare disease by improving access to care, reducing the burden of coordinating their care and improving access to the information they need to live their lives. ▪ The Digital Front Door work will be a key enabler for people interacting with health and social care services in Scotland. This development will aim to allow anyone to book or rearrange appointments, order prescriptions, update their details and generally conduct routine 'transactions' online. This will support better coordination of care for people living with a rare disease and provide the ability for people to use digital products and services to manage their condition. This means being able to access health assessments, diagnosis, monitoring and treatments, making it an option for everyone with a long-term condition to use digital tools. This will be crucial to all of the priorities of this Framework in the short, medium and long term. The response to the Covid-19 pandemic has accelerated the pace of change across health and social care, with services moving quickly and innovatively to provide better access to flexible and digitally enabled support. For many people, this has increased choice and flexibility. For services, it has eased pressures, freeing up time and capacity for services which cannot be delivered digitally. One of those advancements is the rapid expansion of Near Me, also known as Attend Anywhere. This is a safe and secure NHS video consulting service that enables people to attend appointments from home or wherever is convenient. In March 2022, we reached 1.5 million Near Me appointments across Scotland, saving an estimated 49 million travel miles for patient, families and staff.

	▪ Our aim is to continue to provide safe, person-centred and sustainable care through video consulting. Where appropriate clinically and for the individual, everyone should have the choice of attending appointments via an easy and convenient Near Me video call. ▪ We need to make sure that efforts to add more Digital elements into the health and social care system are proportionate to ensure that nobody is left behind, while meeting the expectations of those who want to interact in this way. Digital Front Door will be an iterative development with the first release expected in 2023/24. There will be a programme of engagement as part of the development process, and we will seek participation from the rare disease community to ensure that they are included in this process in the short and long term. ***Action 17: What does this mean for people living with a rare disease?*** The use of new digital elements in healthcare consulting can save on travel, and allow appointments to be conducted in the comfort of a person's own home. Remote consultations such as Near Me video calling should be offered as a choice if it is appropriate for the person and their condition, with the option of an in-person appointment if they prefer. **Action 18: Clinical Research for Rare Disease** Clinical research for rare diseases presents a number of challenges for Scotland, but we know how valuable this is to patients. Such challenges include the distances involved between clinical research centres and the low population density, factors which make equitable access to clinical trials more difficult to achieve. At the same time, the Network of Clinical Research Centres in Scotland, and the development of the Congenital Anomaly Register (CARDRISS) both provide an opportunity to develop new approaches that can improve access to interventional and observational clinical studies for patients. In parallel to improving access to research for people with rare disease, there has been rapid evolution in genomic technology that has the potential to make significant improvements to health of the Scottish population. The development of a strategy for genomics will be highly relevant for the considerable proportion of rare disease that has a genetic basis. We will therefore focus on three areas: **Develop a Scottish Register for Rare Disease** ▪ As covered in Action 3, in the short term, we are committed to consolidating the registration of congenital conditions covered by EUROCAT through the national congenital and rare condition registry service, CARDRISS. In time, we are also committed to extending the scope of the CARDRISS register to cover additional congenital and rare conditions covered by the pregnancy and newborn screening programmes. ▪ Over the medium term, we will work with CARDRISS to develop plans for further extension of the registry service to cover a wider range of rare conditions affecting children and adults. We will work with the registry services in England, Wales, and Northern Ireland to ensure alignment across the UK in this work where feasible and beneficial. ▪ Development of new national data returns providing information on the results of germline genetic testing (summary results, not full DNA sequencing data) from clinical genetic laboratories to Public Health Scotland will be critical to both consolidating current registration of congenital conditions and allowing CARDRISS to cover other rare conditions. We will work with CARDRISS, the team procuring a new information system for labs across Scotland, and the SSNGM to develop these new genetic testing data returns. ▪ Strengthening national data on congenital and rare conditions through CARDRISS will provide many benefits, improving our understanding of specific conditions, supporting policy and service development, and enabling research, including through identification of individuals who may benefit from inclusion in clinical studies. Fit-for-purpose ethical safeguards will need to be developed which protect patients, but facilitate access to data, within the existing governance structure. As noted under Action 3, development of new national data returns and extending the remit of CARDRISS will require investment, which we will consider as part of our future budgetary considerations.

	Improve networking of research across Scotland ▪ We have established a collaborative group with representation that includes clinical investigators, NHS research Scotland and industrial partners. This group will identify the barriers to a "One Scotland" approach to conducting clinical research. Suggested improvements are expected to include an improved governance structure that facilitates referral of patients to studies between regions and a hub and spoke model for the organisation of clinical trials. ▪ We will also explore the development of a Rare Disease Platform for observational research in rare disease that allows integration with the NIHR UK Rare Genetic Disease Research Consortium Agreement. **Develop Genomics research infrastructure** ▪ The most common clinical indication for whole exome or whole genome sequencing in Scotland is for the diagnosis of rare disease. The Rare Disease Implementation Board will, with the new Scottish Strategic Network for Genomics Medicine, seek to deliver safe storage of sequence data within a data system that includes research functionality, but also permits reanalysis of extant sequence data as knowledge improves, providing an increased diagnostic return on testing. ***Action 18: What does this mean for people living with a rare disease?*** Engaging with the wider research landscape in this way will enable access to more studies of benefit to people living with rare diseases. Increased research into rare diseases, and linking this with our genomics offering, will lead to faster diagnoses and help identify new treatments. **Monitoring and Evaluation** We recognise that measuring outcomes for patients, carers and families will be difficult. However, measuring the success of our actions in the short to medium term will be achieved in different ways, depending on what needs to be measured. Work such as better signposting of awareness-raising resources can be measured by assessing their take-up among healthcare professionals, and professional and patient reported improvements in the time taken to diagnose. We will look to develop metrics by which to measure the success of our various actions, such as patient-reported outcome measures.
Governance and organisational structures	**Governance and Oversight Groups** Once those four priorities [*Note: the priorities of the UK Rare Diseases Framework*] had been identified through engagement, and needed to be turned into action, groups were put in place that would govern and enable the development of our response to the Framework. At the UK-wide level, these groups are the UK Rare Disease Framework Board, which oversees our response to the Framework, and the UK Rare Disease Forum, which is more focused on engagement. Representatives from all four nations have been attending these meetings to ensure that we continue to collaborate as four nations wherever appropriate, and to oversee the development of our four Action Plans. We introduced a 'deep dive' format to the Forum meetings, so that all the representatives could tackle a particular key priority in depth and hear from various spheres of expertise on what resources are available and what improvements could be made. To oversee Scotland's specific response to the Framework, our Rare Disease Implementation Board (RDIB) was formed, bringing together those with clinical expertise, representatives of patient advocacy groups and other NHS Scotland and third sector representatives to work on the development of our Action Plan. **Implementation** As health and social care is devolved across the UK, each Action Plan will be implemented in a different healthcare system. We will work with NHS Scotland Boards, and also with NHS Scotland's National Services Division (NSD) to ensure that the actions required to improve the lives of people living with rare diseases can be embedded into standard practice across Scotland. NSD are particularly important here as

	they deal with national and specialist services for small patient groups, which is often the case for the care and treatment of rare diseases. The "Once for Scotland" strategy that NSD apply to their services will also help with better coordination of care. NHS Education for Scotland (NES) are a national Board within NHS Scotland, and the education and training body for NHS Scotland. This is important when we consider the Awareness Raising priority from the Framework: where do health and social care professionals go for training and information resources, and how can we tap into these resources to increase the information available for rare diseases? We have established a working relationship with NES, who are also represented on RDIB, and we will continue to work with NES on strengthening and signposting rare disease information resources, as described in the Awareness Raising actions. NHS Inform is Scotland's national health information service, which aims to provide the people of Scotland with accurate and relevant information to help them make informed decisions about their own health and the health of the people they care for. NHS Inform hosts information about a variety of health conditions, but until now very little regarding rarer conditions. We recognise that with over 7,000 rare diseases it is not feasible to have information about them all, but we want to have some information about rare diseases featured on NHS Inform, and we will draw on the expertise of our RDIB membership to explore what this should be. Third sector partners will also be key to implementing the actions from our Plan. Organisations such as Genetic Alliance UK and Medics 4 Rare Diseases, as well as the Office for Rare Conditions (a University of Glasgow-led project, with some charitable funding) all have experience in developing information resources, and we will continue to draw on their expertise and consider ways in which their work can be better signposted for healthcare professionals. **Next steps** We will continue to work with our counterparts in the other UK nations to discuss and work together on the implementation of our actions plans. This knowledge-sharing will help us all to maximise the impact of our actions, both in our own nations and collaboratively. We will continue to share our progress at the meetings of the UK Rare Diseases Framework Board and elsewhere. Throughout the lifespan of the Framework and our Action Plan, we will continue to engage with people living with rare diseases. We know that your lived experience is the most valuable in informing our work on what challenges need to be addressed, and it will be crucial to keep the rare disease community informed on the progress being made. We will keep working with Genetic Alliance UK and other key partners to schedule further engagement opportunities at which we can discuss our progress with you and identify further priorities for the future.
Funding model	*Mentioned under Action 1:* The Scottish Government will support this strategy through significant investment, with £5 million committed for 2022/23 alone, previous investment of £8 million since 2017. This is in addition to almost £20 million of funding allocated to the four genetic laboratories annually in Scotland by NHS Boards through NHS National Services Division (NSD) commissioning arrangements. *Mentioned under Action 3:* Initial funding to establish CARDRISS was provided by the Scottish Government to NHS NSS Information Services Division (ISD) and latterly to Public Health Scotland (PHS), the current home of CARDRISS, over the three-year period October 2018 to March 2022. We will work with PHS to understand the options to expand CARDRISS. Extensions are likely to require financial investment by the Scottish Government, which we will consider as part of our future budgetary considerations.
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***

Screening programmes (including newborn screening)	*See Actions 2 and 3.*
Personalised medicine, genomics, genetic counselling	*See Actions 1, 9 and 18. Also underpinning theme of 'Wider policy alignment'.*
Models of care/care pathways	*See Actions 4, 9, 10, 12, 13, 14, 15, 17.*
Workforce	*See Actions 1, 6, 7, 8, 15*
European Reference Networks	Not mentioned.
EU alignment and participation	*See Action 3 – references to European Registry of Congenital Anomalies and Twins (EUROCAT).*
Health information (including rare disease registries)	*See Actions 3, 4, 11, 17, 18. Also underpinning themes of 'National and international collaboration' and 'Digital, data and technology'*
Orphan medicines	*See Action 16.*
Rare disease research	*See Actions 2, 3, 18. Also underpinning theme of 'Pioneering research'.*
Alignment beyond the healthcare sector	*See underpinning theme of 'Wider policy alignment'.*
Any additional information (for example, background to the strategy or strategy development)	**Introduction** The Scottish Government worked closely with the UK Government, along with the other devolved nations, to produce a new UK Rare Diseases Framework. The Framework builds on progress across the 51 commitments of the 2013 UK Strategy for Rare Diseases, whilst recognising new challenges and continued room for improvement. The 2013 Strategy was a collaborative vision – between the four nations of the UK as well as between government, the NHS, research and industry. The new Framework, in the same way, forms the basis of how we will work together to improve the lives of people living with a rare disease and those who care for them. It has identified the key government priorities for rare diseases and created a vision for the future shared by all four UK nations.

	The themes which emerged from the National Conversation on Rare Diseases have also been integral in developing both the UK Framework and Scotland's Action Plan. This survey was carried out UK-wide by the Department for Health and Social Care. Over 6,200 responses were received from people living with a rare disease, clinicians, researchers and industry. Over 400 were received specifically from Scotland. Scotland's Rare Disease Implementation Board (RDIB) have considered this evidence base – which includes patient group representatives as well as industry, research and healthcare professionals – to identify where the Scottish Government can build on the progress made under our 2014 Implementation Plan, It's Not Rare to Have a Rare Disease. **Engagement events with the Rare Disease Community** Our patient engagement programme in the development of this Action Plan was twofold. One strand of this was to create a formal advisory group, which became known as our Patient Voices Advisory Group. The membership was drawn from both representatives from patient advocacy groups, and from people with lived experience (and/or familial experience) of a rare disease. The group first met in December 2021. The meetings so far have been extremely helpful in identifying what matters to the rare disease community, what challenges they face and what their priorities are in their treatment and care. We recognise the difficulties and strain on individuals and small organisations in engaging on many platforms. As a result, our Voices Group hasn't perhaps had the turn out we would expect. However, we are reviewing our Patient Voices Advisory Group with Genetic Alliance UK to ensure it works and our methods for engagement do not create an unnecessary burden. The other main strand of our engagement with the rare disease community has been through a more informal series of online events. Like the chairing of our Advisory Group, this has been led by led by Genetic Alliance UK. These events have provided an open platform for discussion and sharing of information and lived experience, as well as a chance for Scottish Government officials to share information about this Action Plan during its development. Patient feedback from these events, and from the meetings of the Advisory Group, has directly informed the structure and priorities of this Action Plan, and will continue to do so in future publications and the actions we take forward. At the beginning of each chapter of the plan, a summary of the feedback is represented in a graphic. We're keen to demonstrate the feedback we received and ensure our action plan is reflective of what we heard.

Key: UK: United Kingdom; NHS: National Health Service; SMA: Spinal Muscular Atrophy; CSO: Chief Scientist Office; UK NSC: UK National Screening Committee; CARDRISS: Congenital Conditions and Rare Diseases Registration and Information Service for Scotland; ISD: Information Services Division; EUROCAT: European Registry of Congenital Anomalies and Twins; PHS: Public Health Scotland; IMDs: Inherited metabolic disorders; NES: NHS Education for Scotland; CPD: Continuing Professional Development; CPG: Cross Party Group; CONCORD: The Coordinated Care of Rare Diseases; ACPS: Anticipatory Care Plans; SMC: Scottish Medicines Consortium; RDIB: Rare Disease Implementation Board; ISD: Information Services Division; NSS: National Services Scotland.

Table B29. Data extracted for the United Kingdom (UK Rare Diseases Framework).

UK	Strategy information
Author(s) **Title**	Department of Health and Social Care The UK Rare Diseases Framework[29]
Timeline	2021-2026 (Published 9 January 2021. Priorities for the next 5 years, at which point it will be reviewed.)
Overall aim(s)	The UK Rare Diseases Framework aims to ensure that the lives of people living with rare diseases continue to improve. We will work across the 4 nations of the United Kingdom to ensure that rare disease patients receive the best possible care, building on the commitments in the UK Strategy for Rare Diseases and major advances in the diagnosis and treatment of rare diseases. This framework will develop positive change in how we diagnose, treat and care for patients with a rare disease.
Themes and or priorities	**Priorities** 4 key priorities (and associated visions) have been identified for the next 5 years, which have been highlighted as major challenges by the rare disease community. **Priority 1: helping patients get a final diagnosis faster** Vision: Our vision is for rare disease patients across the UK to get a final diagnosis faster and for research into previously unrecognised conditions to identify new rare diseases and provide new diagnoses. **Priority 2: increasing awareness of rare diseases among healthcare professionals** Vision: Our vision is for healthcare professionals to have an increased awareness of rare diseases and use of genomic testing and digital tools to support quicker diagnosis and better patient care. **Priority 3: better coordination of care** Vision: Our vision is for rare disease patients to experience better coordination of care throughout the patient journey. **Priority 4: improving access to specialist care, treatments and drugs** Vision: Our vision is for rare disease patients to have improved access to specialist care, treatments and drugs. **5 underpinning themes have also been outlined:** In order to achieve the above outcomes, we recognise that there will need to be a range of supporting activities across the health and social care system. To support these key enablers, 5 underpinning themes have been identified in which work will continue to be progressed to support the priorities of the framework and improve the lives of those living with rare diseases. ▪ Patient voice ▪ National and international collaboration ▪ Pioneering research ▪ Digital, data and technology ▪ Wider policy alignment ▪ **Patient voice** Patients, their families and carers, and the organisations that represent them live with the realities of a rare disease every day. They have a great amount of knowledge and lived experiences to share which can be hugely valuable to policy makers and service providers when

	designing services for rare disease patients. We will continue to put the patient voice at the heart of its decision making and collaborate closely with patients and patient organisations. Therefore, any commitments will be developed in consultation with patient representatives, giving particular consideration to ensuring representation from those whose voices can often go unheard, including patients from Black and Minority Ethnic (BAME) or disadvantaged backgrounds. ▪ **National and international collaboration** Due to the small numbers of patients with individual rare diseases, both national and international collaboration is absolutely essential to support research and patient care, particularly for ultra-rare diseases with only a few patients in the UK. It is only through working together as all 4 nations of the UK, with our European neighbours and international partners that we will be able to undertake robust research and develop the best care for rare disease patients. We are committed to continuing collaboration with the rare diseases community across the world including patients, doctors and industry to share knowledge and ideas to improve outcomes. ▪ **Pioneering research** The UK is a global leader in scientific research and innovation, attracting international industry investment with world class life sciences and research infrastructure. Scientific advancements have underpinned many of the recent breakthroughs for rare disease patients and harnessing the potential of cutting-edge science to better understand the underpinning disease mechanisms of rare conditions and enable development of new treatments will be vital to build on this progress. This year the UK Government published the UK Research and Development Roadmap outlining plans to revitalise UK research and development and have set out an ambition to increase public funding for research and development, including for rare diseases, to £22 billion per year by 2024/25 and to reach 2.4% of GDP spent on research and development by 2027. Through the UK's thriving life sciences sector, research councils, research charities, the National Institute for Health Research in England, the Chief Scientist Office in Scotland, Health and Care Research Wales, and the Public Health Agency's Health and Social Care Research and Development division in Northern Ireland, we will continue to support and invest in innovative research for rare diseases and ensure that the outcomes are translated into frontline clinical care. ▪ **Digital, data and technology** Similar to advances in science, new technologies also have the ability to revolutionise care for patients across the NHS with particular benefit for rare disease patients. For example, telemedicine and video conferencing are already being trialled in parts of the NHS and have the potential to significantly reduce the burden on rare disease patients and their families travelling to different appointments across the country. Digital and online resources, examples of which are already provided by some patient organisations, could also prove invaluable to healthcare professionals as a resource for understanding how best to care for a rare disease patient. When working towards the aims of the framework, we will utilise the benefits technology can bring to rare disease patients and consider how digital tools could be appropriately used to improve efficiency and patient experience and support research. Effective data interoperability and the ability to easily share and access patient data and registries will also be important for supporting multidisciplinary teams discussing patient care and researchers developing new treatments. Robust rare disease registries, such as the National Congenital Anomaly and Rare Disease Registration Service (NCARDRS) in England, the Congenital Anomaly Register and Information Service (CARIS) in Wales and Congenital Anomalies and the Rare Diseases Registration and Information Service for Scotland (CARDRISS) in Scotland are also crucial in supporting researchers, clinicians, patients and service commissioners and can also be key to identify non-genetic rare diseases, which do not benefit from screening programmes or genomic testing.

	▪ **Wider policy alignment** Improving the lives of those living with rare diseases goes beyond healthcare. Due to the nature of their condition, many rare disease patients require housing adjustments, social care, financial aid, mental health support and special educational needs support. Wider policy development in these areas must reflect the needs of those with rare conditions. Caring for rare conditions also requires specially trained staff, including nurses, care-workers and consultants. With the increasing use of genomics in healthcare, the need for staff trained in genetics and genomics is particularly great. Therefore, workforce and long-term succession planning must also consider the needs of rare disease patients in both health and social care. As well as addressing the priorities in the UK Rare Diseases Framework, we will work to ensure that the needs of rare disease patients are recognised in wider policy development, whether that be mental health, social care, specialist educational support, or long-term workforce planning. Given the importance of genomics in improving diagnosis for some rare diseases, and to support new research unto potential treatments, the framework will align closely with Genome UK, the Government's strategy for genomic healthcare, as well as other relevant strategies and policies. Policy documents on wider work which will have a positive impact on the support available to rare disease patients, including work to tackle health inequalities, will be signalled to in each nation's action plan.
Targets (if specified) and measurement method(s) (where available)	**Priority 1: helping patients get a final diagnosis faster** Our vision is for rare disease patients across the UK to get a final diagnosis faster and for research into previously unrecognised conditions to identify new rare diseases and provide new diagnoses. **Priority 2: increasing awareness of rare diseases among healthcare professionals** Our vision is for healthcare professionals to have an increased awareness of rare diseases and use of genomic testing and digital tools to support quicker diagnosis and better patient care. **Priority 3: better coordination of care** Our vision is for rare disease patients to experience better coordination of care throughout the patient journey. **Priority 4: improving access to specialist care, treatments and drugs** Our vision is for rare disease patients to have improved access to specialist care, treatments and drugs.
Implementation action(s), lead(s) and key performance indicator(s)	**Principles of the UK Rare Diseases Framework** All 4 UK nations have signed up to the UK Rare Diseases Framework and have therefore agreed to collaborate to achieve the outcomes set out above. However, as health is a devolved matter, each nation will deliver these aims in a way which is most effective for their respective populations. Therefore, each nation will set out an action plan detailing the steps they will take to meet the aims of the framework within their own arrangements. In order to ensure cross-border collaboration and maximise the benefits of the framework for the rare disease community, each nation will follow the below core principles when delivering action plans and implementing the framework. Each nation will: ▪ Deliver the aims of the UK Rare Diseases Framework under each of the priorities and underpinning themes: ▪ Consider where action plans can contain specific and measurable commitments under each focus area and regularly review commitments (every 1 to 2 years). ▪ Develop policy commitments with expertise, in close collaboration with patients and others living and working with rare diseases. ▪ Ensure any impacts on health inequalities are considered when developing action plans. ▪ Ensure that the experiences of rare disease patients during the COVID-19 pandemic are reflected in the development of action plans and implementation of framework priorities and themes.

	▪ Ensure that the voice of the rare diseases community is recognised across the system and that work as part of the UK Rare Diseases Framework is aligned with other relevant policy development, such as mental health and social care. ▪ Work collaboratively across nations to share knowledge and best practice. ▪ Review progress made towards the aims of the framework every 5 years and update priorities when necessary. Following the publication of the UK Rare Diseases Framework, all 4 nations will develop action plans which will set out how the priorities identified in the framework will be addressed, taking into account the underpinning themes. These action plans will be developed according to the principles of the UK Rare Diseases Framework and we will work closely with the rare diseases community to ensure the commitments developed are actionable and measurable. Where possible, each nation will aim to publish the action plans in 2021.
Governance and organisational structures	At the heart of these developments has been the empowerment of the patient voice. With the establishment of the UK Rare Disease Policy Board and Forum and groups such as the 100,000 Genomes Project Patient Participant Panel, the Rare Diseases Advisory Group, government has been able to work hand in hand with the rare diseases community to deliver policies centred around the patient experience and need. Ongoing collaboration between patients and policy makers will be vital moving forward in order to build on these successes.
Funding model	*Not mentioned.*
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***
Screening programmes (including newborn screening)	**Priority 1: helping patients get a final diagnosis faster** For people living with a rare disease, getting the right diagnosis is key to appropriate management of their condition. It can enable greater treatment choice and reproductive decision making and can link individuals to vital information and support through patient organisations. However, getting the right diagnosis has been consistently highlighted as one of the most significant challenges faced by both the genetic and non-genetic rare disease community. Currently, it can take years to receive a final diagnosis, and some people living with a rare disease may never receive one at all. This 'diagnostic odyssey' often involves multiple referrals, inconclusive tests, and sometimes incorrect diagnoses before a final diagnosis is obtained. Without the right diagnosis, it is difficult for patients to receive the best treatment to manage the symptoms of their condition and may miss out on treatments that target their underlying disease. Screening programmes identify healthy people in the population who are asymptomatic but have an increased risk of developing a disease or condition. The aim is to detect and provide further tests or treatment at an earlier stage with the objective of improving outcomes. The UK National Screening Committee (UK NSC) advises Ministers and the NHS in all 4 countries on potential screening programmes, appraised against its internationally recognised criteria to consider viability, effectiveness and acceptability. The UK NSC will only recommend a screening programme where this is shown to do more good than harm. Newborn Blood Spot screening is also offered to all babies at 5 days old to test for 9 serious but rare conditions, including congenital hypothyroidism, sickle cell disease, cystic fibrosis and inherited metabolic diseases. While most babies will have a normal result, a small number of babies will screen positive and will be referred for further tests or treatment as required. The UK NSC run an annual open call for new screening proposals, which can include proposals for additions to the Newborn Blood Spot screening. The UK NSC recently reported that there is clear potential for genomics in the testing for many of the conditions currently included in the blood spot test. Together with our world-leading genomic infrastructure embedded in the NHS, this makes the UK uniquely placed to conduct a high quality, large-scale research programme to determine whether and how sequencing should be implemented for screening in newborns.

Personalised medicine, genomics, genetic counselling	**Priority 1: helping patients get a final diagnosis faster** Advances in genomics and diagnostic services have allowed us to make significant strides towards shortening the diagnostic odyssey for many rare disease patients. In the future, we expect that new, validated genomics approaches and diagnostic tools will contribute to further improvements in diagnosis and screening, including improved recognition of which patients should undergo advanced genetic testing. This will be further strengthened by the aim set out in Genome UK to make it easier to return findings from research to better inform clinical practice for rare disease patients. It is also critical to support patients with non-genetic rare diseases, and the healthcare professionals treating them, to reach a diagnosis as soon as possible. We must ensure diagnosis rates continue to improve, including utilising advanced diagnostic technologies and tools where possible.
Models of care/care pathways	**Priority 3: better coordination of care** As many rare diseases are chronic and affect multiple body systems, those living with rare disease, whether diagnosed or undiagnosed, face multiple hospital appointments and complex condition management. The management of their condition may require the expertise of multiple different specialists, who could be spread across different hospitals, and individuals may also have regular interaction with other services such as GPs and social care. Parents of children with rare conditions often face a significant care burden, needing time off work to look after their children and take them to appointments, and there can be challenges in ensuring continuity of care when transitioning between paediatric and adult services. Therefore, coordination of care is essential to ensure care is effectively managed, the burden on patients and their carers is minimised, and healthcare professionals are working together to provide the best possible joined up and high-quality care. There are many potential benefits of using advances in technology and new digital tools to support better care coordination, allowing patients to access services remotely and enabling specialists from across the system to easily share information and discuss tailored care plans. The use of virtual multidisciplinary team meetings, telemedicine, video appointments and alert cards are starting to be implemented across some rare disease services and are all great examples of using technology to support better care coordination. The COVID-19 pandemic has necessitated the use of more virtual appointments, and there is great potential to build on this infrastructure going forward, whilst considering the implications of digital inequalities.
Workforce	**Priority 2: increasing awareness of rare diseases among healthcare professionals** Awareness of rare diseases among healthcare professionals is also raised by the rare disease community as a key challenge. At the start of a patient's journey, the first point of call is often their GP. When faced with a patient with unusual or unexplained symptoms, many GPs will not routinely have knowledge or experience to correctly identify that they are suffering with a rare condition. Similarly, paramedics or A and E staff are not likely to be familiar with correct emergency procedures when a rare disease patient needs emergency hospital care. With over 7,000 rare diseases, no healthcare professional can receive training on every rare disease. It is therefore important that they are aware of rare diseases more widely, alert to considering them, and are provided with the education and resources that can help them recognise rare diseases in patients and be aware of potential specialist treatment needs. With our ambition to create the most advanced genomic healthcare system in the world, healthcare professionals need to be offered opportunities to continue to improve their understanding of genomics, particularly for its application in diagnosing rare diseases. Additional education and training, specific and relevant to their role, will allow clinicians to effectively recommend appropriate tests and be skilled in the interpretation of results to inform patient care. It is particularly crucial for healthcare professionals to be conscious of rare diseases and supported with the right training and materials to know when to consider whether a patient has a non-genetic rare condition, which often rely on a clinical diagnosis.
European Reference Networks	*Not mentioned.*

EU alignment and participation	*See themes – 'National and international collaboration'*
Health information (including rare disease registries)	*See themes – ''Digital, data and technology'*
Orphan medicines	**Priority 4: improving access to specialist care, treatments and drugs** Due to the nature of rare diseases, providing access to safe, high-quality specialist care and treatments can present challenges including some patients having to travel significant distances to access specialist centres. Patients need to have access to expertise in the treatment and care of their rare disease where available and there are opportunities to develop innovative models of care across the healthcare system so that patients have their care delivered as locally as possible. Very few rare diseases have established treatments, but where they do exist, they can be life-changing, significantly improving prognosis and/or quality of life. The development of new treatments by pharmaceutical companies is complex, from understanding the basic science of a disease in small populations to the use of novel clinical trial methodologies, which can be reflected in high drug prices. Assessment of, and access to, rare disease medicines for small patient populations can provide challenges to health technology assessment bodies (such as NICE, Scottish Medicines Consortium and the All Wales Medicines Strategy Group) due to limited and uncertain data and challenges for the NHS in finding the balance between the need for treatment for all patients against fixed resources. The Government recognises the global nature of research and innovation and aims to sustain, improve and foster opportunities for international collaboration. It is essential that the UK can offer an environment that will attract substantial investment in high value life science products of the future, and that will attract discovery scientists from global pharmaceutical companies to the UK. This aligns with ambitions to attract and retain global investment, science, research and innovation talent to the UK that are set out in the UK Life Sciences Industrial Strategy published in 2017 and reiterated in its 2020 update. Ensuring continued development and improved access to specialist expertise, treatments and drugs will require innovation and we must harness opportunities to fully realise our global potential, and to signal our commitment to innovation and collaboration. The UK Research and Development roadmap sets out an ambition for the NHS to take a greater role in seeding and adopting evidence based innovative new treatments, including the work of the Early Access to Medicines Scheme, the Accelerated Access Collaborative and the expansion of the Innovative Medicines Fund, which will be subject to a public engagement exercise in the first quarter of 2021. In addition, NICE is reviewing the methods and processes it uses in the development of its technology appraisal and highly specialised technologies recommendations. NICE is being ambitious in the scope and breadth of this review and will continue to welcome contributions from all stakeholders throughout. The UK is a world leader in science, with a world-class research infrastructure, and an increasing number of innovative drugs and treatments are being developed for rare diseases. It is vital that we continue to collaborate internationally, support researchers and industry to better understand rare diseases, and to develop new affordable treatments, establish their clinical and cost effectiveness, and improve the pathway for rare diseases treatments reaching patients on the frontlines of clinical care.
Rare disease research	*See themes – 'Pioneering research'*
Alignment beyond the healthcare sector	*See themes – 'Wider policy alignment'*

Any additional information (for example, background to the strategy or strategy development)	In 2013, the UK Government and the three devolved administrations published the first UK Strategy for Rare Diseases (the strategy). The strategy represented a step-change in the way we think about rare diseases and respond to the challenges faced every day by rare disease patients and their families. The strategy was widely welcomed by the rare disease community and was a major collaborative milestone, with all 4 nations working together towards common goals to improve the lives of rare disease patients and those who care for them. Since publication of the strategy, there has been much progress to reflect on with new challenges and opportunities emerging. The COVID-19 pandemic in particular has brought many of the challenges faced by the rare disease community into sharp relief. It is vital that the government continues to support those living with and caring for those with rare diseases, many of whom are especially vulnerable to coronavirus through the current and any future pandemics. There will be opportunities to learn from the COVID-19 pandemic and the experiences of rare diseases patients and to reflect on this learning in shaping the broad commitments of this new framework and wider national responses to infectious disease outbreaks. **Our approach** To identify the priorities for the next 5 years, we undertook a programme of engagement to understand the main challenges for those living and working with rare diseases across the UK and how these could be addressed. In October 2019 government launched the National Conversation on Rare Diseases Survey to seek the views of patients, their families, clinicians, researchers and rare diseases patient organisations. The survey ran for 6 weeks and received a remarkable 6,293 responses from the community. The results of the survey can be found at Annex A. Following the survey, an Editorial Board of policy officials, representatives from clinical practice and patient organisations was formed to formally identify and refine the priorities and underpinning themes for the new framework. These ideas were further tested through stakeholder engagement with patient organisations, clinicians, researchers and industry representatives and were put to the UK Rare Disease Policy Board and Rare Diseases Advisory Group for discussion. 4 key priorities have been identified for the next 5 years. Work in these areas will be supported by 5 further underpinning themes which will be vital for delivering results. The UK Rare Diseases Framework is being developed in 2 key phases. **Phase 1** Phase 1 is this document – the UK Rare Diseases Framework. This framework sets out our 4 priorities and 5 underpinning themes for improving the lives of those living with rare diseases across the UK. It sets out a high-level vision for each of these priority areas, shared by all UK nations, providing a strategic direction for the UK's work on rare diseases across the next 5 years, at which point it will be reviewed. **Phase 2** In Phase 2, each nation will develop an action plan, highlighting steps they will take to meet the aims of the framework in accordance with their own arrangements. Health is a devolved matter and therefore each individual nation has the flexibility to deliver the aims of the framework in the way which is most effective for their population. These action plans will be developed in close collaboration with the rare diseases community through additional engagement and will be reviewed regularly (every 1 to 2 years). Importantly, we will work to reduce health inequalities, including taking steps to meet the needs of people with disabilities where these are different from the needs of other people. In the spirit of continued UK collaboration and to ensure best practice across the UK, each nation will follow a set of core principles when delivering action plans and implementing the framework (see page 12).

Key: UK: United Kingdom; NHS: National Health Service; NCARDRS: National Congenital Anomaly and Rare Disease Registration Service; CARIS: Congenital Anomaly Register and Information Service; CARDRISS: Rare Diseases Registration and Information Service for Scotland; UK NSC: The UK National Screening Committee; A and E: Accident and Emergency; NICE National Institute for Health and Care Excellence.

Table B30. Data extracted for Wales (Rare Disease Action Plan).

Wales	Strategy information
Author(s) **Title**	NHS Wales Health Collaborative Wales Rare Diseases Action Plan 2022 - 2026[43]
Timeline	2022-2026
Overall aim(s)	Demonstrating the ongoing commitment to the rare diseases community, and to build on the achievements of the previous strategy, the governments of all four UK nations have worked together with the rare disease community to design a new UK Rare Diseases Framework, which was published in January 2021. This framework identifies the key priorities for rare diseases going forward and creates a vision for the future which is shared by all four UK nations to address health inequalities, improve the quality and availability of care, and improve the lives of people living with rare diseases. To implement the UK Rare Diseases Framework, Wales has developed their own action plan, outlining commitments to meet the priorities of the Framework.
Themes and or priorities	**4 priorities the same as the UK Framework.** **Priority 1: helping patients get a final diagnosis faster** The vision is for rare disease patients across the UK to get a final diagnosis faster and for research into previously unrecognised conditions to identify new rare diseases and provide new diagnoses. **Priority 2: increasing awareness of rare diseases among healthcare professionals** The vision is for healthcare professionals to have an increased awareness of rare diseases and use of genomic testing and digital tools to support quicker diagnosis and better patient care. **Priority 3: better coordination of care** The vision is for rare disease patients to experience better coordination of care throughout the patient journey. **Priority 4: improving access to specialist care, treatments and drugs** The vision is for rare disease patients to have improved access to specialist care, treatments, and drugs.
Targets (if specified) and measurement method(s) (where available)	*Not mentioned.*
Implementation action(s), lead(s) and key performance indicator(s)	The details of the plan are set out for each of the four main priorities. Each section is further supplemented with some background information as to the reasons for the actions in the plan and divided into relevant sub-sections with "colour" coding for easier consideration of the actions. Each action is structured in a similar way: 1. Action 2. Delivery partners / Stakeholders 3. Timeline 4. Measure / Outcome

	Priority 1: helping patients get a final diagnosis faster **Whole Genome Sequencing (WGS) for rare diseases** 1.1 Increase Whole Genome Sequencing testing for rare diseases. AWMGS/WG/WHSSC. 2022/23. Increased number of tests performed. **Whole Exome Sequencing (WES) for rare diseases** 1.2 Return Fetal Whole Exome Sequencing trios testing (FAGP service) to Wales. AWMGS/WG/WHSSC. 2022/23. Number of tests performed/returned to Wales for testing. **Whole Transcriptome Sequencing for rare disease** 1.3 Ensure validation of a whole transcriptome service which will enable better understanding of RNA sequences to determine if a DNA sequence is turned on and whether proteins have changed. AWMGS. 2022/23. Validation of methodology. **Research Eco-system** 1.4 Ensure a consent strategy is developed that enables researchers to securely and safely access routine genomic data generated by AWMGS for translational research purposes. WGP. 2022. Publication of consent strategy allowing improved access to genomic data for research purposes. Increased number of patients entering research studies. 1.5 Engagement with Health and Care Research Wales to ensure access to research studies for rare diseases patients. RDIG/ Health and Care Research Wales. 2022-2026. Increased number of rare diseases patients entering studies. **Prevention and Early Detection** 1.6 Establish a public health and screening system in Wales that uses genomics to strengthen the current biochemical screening, diagnostic and care pathways in those at high risk. UK National Screening Committee, Newborn Genomes Programme, Wales Screening Committee (WSC), GPW, PHW, National Screening Laboratory (NSL), WHSSC. 2022-2026. Increased number of rare diseases diagnosed by screening. 1.7 Explore how genomic testing can continue to be best used in reproductive medicine to support parents to make informed choices. 1. NIPT will be expanded to other reproductive pathways to improve patient outcomes and optimise resource utilisation. 2. Implement a next generation sequencing service to detect genomic alterations when fetal structural abnormalities have been identified on ultrasound scan. AWMGS, PHW, WSC. 2022-2026. Number of tests performed. **Service/Digital/Technical Infrastructure** 1.8 Ensure horizon scanning for commissioning requirements to inform the current National Genomic Test Directory for rare and inherited disease. AWMGS/ WHSSC. 2022-2026. Improved test availability. ***Priority 2: increasing awareness of rare diseases among healthcare professionals*** **Lead Clinician for Rare Diseases** 2.1 Monitor ongoing role and work programme of Clinical Lead and Clinical Champion for rare diseases to raise profile of rare diseases. RDIG, health boards, trusts and all stakeholders. April 2022. Review of achievements of the role by RDIG, NHS Wales Health Collaborative and WG after two years in post. **Education and Shared Learning** 2.2 Survey qualified HCPs, undergraduates on their understanding and learning needs in rare disease. Use results to develop training and development plan from baseline information on HCP understanding of rare diseases. HEIW M4RD (undergraduate project in planning stage Universities Rare Diseases Nurses Network (RDNN) RDNN. 2023/24. Within two years: Improved awareness of rare diseases amongst healthcare professionals.

	2.3 Incorporate rare diseases module in the undergraduate curriculum for medical students. RDIG, HEIW, Universities. 2022 -2026. Improved awareness of rare diseases amongst medical students. 2.4 Continue to develop active partnerships with patients and patient advocacy groups (PAGs). HEIW, Welsh training institutions, Genetic Alliance, RDIG, WGP. 2022-2026. Increased number of people with a rare disease involved in course delivery. 2.5 Recognise and celebrate rare disease day in secondary and primary care. RDIG, Genetic Alliance. Annually Reporting to RDIG on health board/trust programmes by their representatives. 2.6 Improve health professional awareness through joint working between primary/secondary and tertiary care such as local pilot (Hywel Dda) Webinars for General Practitioners with AWMGS. AWMGS, RDIG, Hywel Dda UHB. 2022. Improved awareness of rare diseases in primary care. 2.7 Ongoing programme of WGP education and engagement with HCP and students including Genomic Counselling role (across Welsh Health Boards and HEIs) including precision medicine. WGP GPW AWMGS Rare Disease Community, Wider genomics community. 2022/23. Metrics (attendance) and evaluation of activities including number of workforce engaged. **Improving Awareness of Rare Diseases with Data** 2.8 Expand CARIS expansion to include adults affected by rare conditions. CARIS to collaborate with a small number of patient organisations to pilot research projects and generate patient data for a new adult register and allowing patients to self-report. CARIS, RDIG, WG, Genetic Alliance. 2022/23. Increased number of new conditions incorporated into the CARIS programme. 2.9 Confirm and regularly share the agreed metrics to be used for rare diseases patients, providing data to each UHB/Trust to raise awareness of performance in the UHB's/Trusts by RDIG. RDIG and relevant stakeholder groups with health board/trust representatives. 2022/23. Maintain and improve compliance. 2.10 Consider collection of rare diseases data at both a National All-Wales level drilled down to lower-level geographies (such as UHB/Trust footprint) where numbers of patients with specific diseases allow. RDIG (health board/trust members) and CARIS. 2022-2026. Improved access to specific condition- based data on a geographical basis. ***Priority 3: better coordination of care*** **Pathways of Care** 3.1 Ensure implementation of transition guidance with all paediatric patients transitioning to adult services should have a named worker and digital care plan linked to a patient passport. RDIG, WHSSC, WG 2022-2026 Improved transitional care for rare disease patients. 3.2 Establish Rare Diseases as a "Community of Practice" and develop example/exemplar clinical pathways for rare disease conditions, including MDT involvement. RDIG, Rare Diseases Clinical Lead WG, Clinical Programme Director for the NCF 2022 (create first pathway) 2023-2026 (continue pathway development) Improved patient experience and improved pathways of care. **SWAN Clinic** 3.3 Continue to build the establishment and assess/evaluate SWAN clinic. WG, WHSSC, Cardiff and Vale UHB 2021 - 2023 Improved patient outcomes/ diagnosis. 3.4 Develop suitable PREM, PROMs for use in evaluation in the SWAN clinic with potential use across all rare disease patients. WHSSC, Cardiff and Vale UHB 2022 Improved patient reported outcomes/ Experiences. **Digital Patient Record** 3.5 Establish an easily used "app" to enable a "patient passport" for rare disease patients RDIG, Betsi Cadwaladr UHB, Life Sciences Hub Wales, Industry partners. 2022 All rare disease patients have access to a 'patient passport'. **Mental Health Services**

3.6 Ensure the mental health needs of rare disease patients and carers are considered as part of the overall mental health strategy for Wales and consider whether further guidance is needed such as a good practice guide for rare disease patients. RDIG, health boards, WG 2022 -2023 Improved mental well-being for rare disease patients.

Priority 4: improving access to specialist care, treatments and drugs

Access to Medicines and Treatment

4.1 Ensure continued access to orphan and ultra-orphan medicines in Wales. AWTTC, RDIG and WHSSC 2022-2025 Improved access to orphan and ultra-orphan medicines.

4.2 Ensure horizon scanning for new medicines for patients in Wales to allow timely awareness of new products and availability of new medicines. RDIG (health board representatives), AWTTC 2022/23 Improved access to new medicines and appropriate uptake.

4.3 Monitor uptake of new rare diseases medicines and prescribing. RDIG, AWTTC 2022 Improved access to new medicines for rare disease patients.

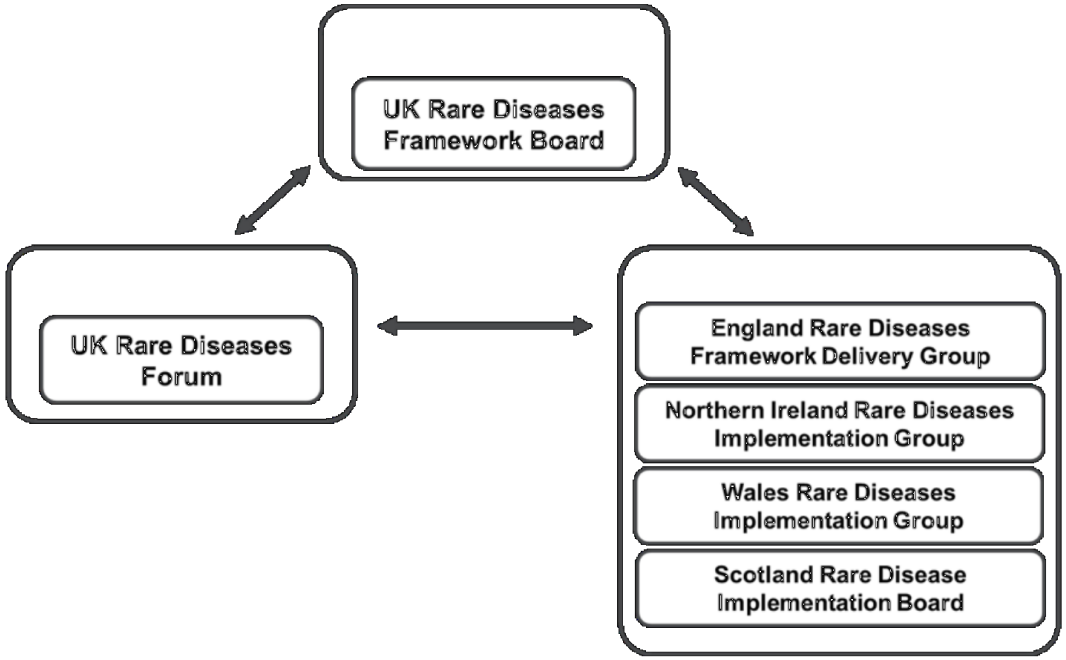
4.4 Continue to develop improvements in the monitoring of use of medicines for patients with rare diseases including Blueteq. WHSSC, AWTTC, RDIG 2022-2026 Improved access and effective use of medicines.

Access to Specialist Care

4.5 RDIG to continue to work with WHSSC and HEIW to ensure appropriate consultant specialist services in Wales. (Note some services will need to be provided outside Wales for specific conditions to ensure appropriate expertise and critical mass of patients). RDIG, HEIW, WHSSC 2022-2026 Rare disease patients have access to appropriate specialist opinions.

Abbreviations:

ATMPs	Advanced Therapy Medicinal Products
AWGL	All Wales Genomics Laboratory
AWMGS	All Wales Medical Genomics Service
AWTTC	All Wales Therapeutics and Toxicology Centre
CA	Congenital Anomalies
CARIS	Congenital Anomaly Register and Information Service
CES	Clinical Exome Sequencing
GPW	Genomics Partnership Wales
HSST	Higher Specialist Scientist Training
ID	Intellectual Disability
MDT	Multi-disciplinary Team
M4RD	Medics 4 Rare Diseases
NCF	National Clinical Framework
NIPT	Non-Invasive Prenatal Testing
NSL	Newborn Screening Laboratory
PAG	Patient Advocacy Group
PEG	Patient Empowerment Group
PHW	Public Health Wales
PREM	Patient Reported Experience Measures
PROM	Patient Reported Outcome Measures

	RDIG Rare Diseases Implementation Group **RDNN** Rare Diseases Nurses Network **SNP** Single Nucleotide Polymorphism **STP** Scientist Training Programme **SWAN** Syndrome Without a Name **UHB** University Health Board **WSC** Wales Screening Committee **WES** Whole Exome Sequencing **WG** Welsh Government **WGP** Wales Gene Park **WGS** Whole Genome Sequencing **WHSSC** Welsh Health Specialist Services Committee **WINGS** Wales Infants and Children's Genome Service **WSL** Welsh Screening Laboratory
Governance and organisational structures	

	In Wales, the RDIG has oversight for the development of a Welsh Action Plan. As shown above, the UK-wide UK Rare Diseases Framework Board provides strategic oversight and facilitates alignment of policy across the four UK nations. The UK Rare Diseases Forum, also UK-wide, provides a means of engagement with the community. Through the online platform it provides an opportunity to engage continuously with a broad range of people from the rare disease's community, providing an opportunity for discussion and feedback, as well as a source of updates on progress and related initiatives. The Wales Rare Disease Implementation Group (RDIG) works with health boards and partner organisations acting as the mechanism for the development and oversight of the action plan for Wales. A UK wide newsletter is also produced which provides policy updates on implementation and progress as well as relevant news on rare disease developments in each country. **Monitoring and Evaluation** RDIG will continue to meet regularly to report on progress. This will include a process of constant review and any changes to the plan will be considered on an annual basis. This will include those actions completed during the year and timescales for those not completed and barriers to completion. A number of developments will be subject to agreement of available resources and ongoing/successful business cases. By developing the plans in a clear way with: 1. Actions 2. Delivery partners / Stakeholders 3. Timeline 4. Measure / Outcome It will provide a platform for objective measurement of the success of the plan. Measuring outcomes for patients, carers and families is always going to be difficult. As part of a piece of work flowing from the SWAN pilot, we are looking to develop PREMs, PROMs and patient experience surveys for patients with rare diseases. That should be a piece of on-going work to roll out across our services and is included in the plan. Patient stories are a powerful way to continue to work with patient groups to tell both positive and negative experiences. The partnership and collaborative working with patients are essential to learn whether we are making real differences to the lives of patients, carers, and families in all four priority areas. RDIG and partners will work with the other UK four nations and their equivalent groups to ensure that best practice is considered for implementation in Wales. Likewise, Wales and its rare diseases community will actively take part in joint working with the other UK four nations to share the work from Wales.
Funding model	RDIG has sought to bring together stakeholders and with university health board (UHB) and Trust representatives across Wales and Welsh Government to raise the profile of rare diseases since the first Welsh Rare Diseases Plan. It is particularly pleasing that collectively the members of RDIG have successfully secured Welsh Government (WG) funding for co-ordinator support, a new all-Wales Clinical Lead for Rare Diseases, and also setting up a two-year pilot for a Syndrome Without a Name Clinic (SWAN). The SWAN clinic initiative is an all-Wales initiative to assess (with a two-year pilot) the opportunity for formally establishing this service. This assists a more rapid diagnosis but also aims to improve co-ordination of care and support for patients for whom there is no diagnosis.
References and or links to relevant initiatives	***(If already extracted above, redirect to appropriate section(s). If no information is included in the strategy, list as 'not mentioned'.)***

Screening programmes (including newborn screening)	*See 'Implementation action(s), lead(s) and key performance indicator(s)' section – Priority 1.* **Priority 1 - Helping patients get a final diagnosis faster** **Background** In taking forward the Welsh UK Rare Diseases Action Plan it is essential that priorities for building upon recent advances in genomic diagnostic technologies to help patients receive a final diagnosis faster and reduce the 'diagnostic odyssey' are included in the plan. In April 2019, the AWMGS introduced rapid whole genome sequencing in newborn and paediatric intensive care units as the Wales Infants and Children's Genome Service (WINGS). To date a genetic diagnosis has been found in about 45% of patients, allowing for diagnostic and prognostic information to inform patient management. A detailed three-year genomics delivery plan (2022 - 2025) for Wales has been developed to significantly enhance the ability of genetic techniques to improve the ability of patients to get a final diagnosis faster. A roll-out of whole genome and exome sequencing to patients with a suspected rare disease is planned. The ambition is to sequence five thousand genomes annually within the next five years. Raising of awareness of rare diseases (priority 2) and the methods of diagnosis to ensure the capacity is used will be required. Further understanding of the genetic causes of illness will be achieved by validation of a whole transcriptome service. This will enable better understanding of RNA sequences to determine if a DNA sequence is turned on and whether proteins have changed. In April 2018, the AWMGS launched Non-Invasive Prenatal Testing (NIPT) as part of the antenatal screening pathway for pregnant women in Wales who are found to have a higher chance of a child with Down's, Edwards and Patau syndromes. The NIPT is offered as an alternative to an invasive test. Wales was the first UK nation to introduce NIPT. Building upon this, NIPT will be expanded to other reproductive pathways to improve patient outcomes and optimise resource utilisation. An infrastructure providing suitable service, digital and technical infrastructure will be needed and resourced with a suitable financial structure.
Personalised medicine, genomics, genetic counselling	*See 'Implementation action(s), lead(s) and key performance indicator(s)' section – Priority 1 and 'Newborn screening'.*
Models of care/care pathways	**Priority 3 Better coordination of care** **Background** Care coordination in transition services needs to be improved, particularly between paediatric to adult care and between diagnosis to treatment of rare conditions in line with Welsh Government's 'Transition and handover from children's to adult health services' guidance published in February 2022. Commissioning agreements should include the provision of care co-ordinators for transition between paediatrics and adults and specialist services generally. All paediatric patients should receive a named worker and care plan to support them through this process. A digital care plan that can be shared with professionals across health, social care and education and controlled by the patient or family would be of greatest benefit. This should link with any technology utilised to support Priority 1 and the patient passport mentioned later in this section. Sharing of data and communication between healthcare professionals and patients in respect of cross border healthcare and treatment must be addressed. Commissioning of specialised services must include funding for dedicated care coordination support for patients and their families and to act as a liaison between the patient and centres/ professionals in Wales and the specialist centre. A major opportunity for the rare diseases community is through the implementation of National Clinical Framework published in March 2021. It is a vital part of a much broader effort that was described in 'A Healthier Wales'. It sets out a vision for how clinical services in our

	NHS fit into that wider picture and how we can begin to realise ambitions through the development of a learning health and care system. It seeks to unleash the revolution and recognises that greater central direction is needed to make that behaviour and philosophy a reality. The Framework sets out a health system that is co-ordinated nationally and delivered locally or through regional collaborations such as potentially a rare diseases Community of Practice. This includes producing the principles of pathways of care for rare diseases patients and some example/exemplar pathways. Pathway development should consider the inclusion of 'red flags' for clinicians and will be a means by which there is improving co-operation between primary, secondary, and tertiary care. There should be recognition in these pathways of the provision of multi-disciplinary care (the need for co-ordination of psychological services is recognised) and time for multi-disciplinary team (MDT) meetings. The SWAN clinic initiative is an all-Wales initiative to assess (with a two-year pilot) the opportunity for formally establishing this service. This assists a more rapid diagnosis but also aims to improve co-ordination of care and support for patients for whom there is no diagnosis. In addition, joint work between RDIG, Betsi Cadwaladr UHB and industry is being enabled by funding from the Welsh Health Hack (Life Sciences Hub Wales) to develop a 'patient passport' for rare diseases patients to improve patient experience. Addressing the mental health needs of rare disease patients is fundamental part of improving their well-being and care. Consideration must be given as to how best to address these needs which could include establishing good practice guidelines to ensure the mental health needs of rare diseases patients are recognised and incorporated into "routine" care for patients. Advice and recommendations are available already as part of the Rare Disease UK publication "Living with a rare condition: the effect on mental health (2018)".
Workforce	**Priority 2 Increasing awareness of rare diseases amongst healthcare professionals** **Background** An important development to improve clinical engagement (funded by Welsh Government) is the appointment, in April 2022, of a senior clinician as Clinical Lead and Clinical Champion for rare diseases working with RDIG, health boards, trusts and all stakeholders to raise the profile of rare diseases and initiate appropriate workstreams in discussion with partners. ▪ To understand and improve current levels of 'healthcare professional awareness', a number of actions are required: ▪ Improve the healthcare workforce's current basic knowledge of rare disease including what a rare disease is, national statistics, common challenges in rare disease, where to go for information ▪ Improve patient-reported experiences of interacting with Health Care Professionals (HCPs) ▪ Build the systems required to support healthcare professionals to understand and play their role in their rare disease patient's journey. Since 2017, WGP has been a strategic partner of GPW and member of its Workforce and Training Implementation Group. WGP has a well-established genetics and genomics-related programme of Education, Engagement and Involvement initiatives, which includes raising health professional awareness of rare, genetic, and undiagnosed conditions. Integral to this programme is the involvement of those affected, to ensure the lived experience informs the education of health professionals, as well as empowering those taking part. Going forward, this will also be an essential aspect of the new Genomics Delivery Plan for Wales and the Rare Diseases Action Plan. **Priority 4 Improving access to specialist care, treatment, and medicines.** **Background** There must also be recognition of the need for a sustainable workforce including Consultant Specialists in Wales requiring workforce planning by HEIW and WHSSC to ensure access to specialist care.
European Reference Networks	*Not mentioned.*

EU alignment and participation	*Not mentioned.*
Health information (including rare disease registries)	*See 'Implementation action(s), lead(s) and key performance indicator(s)' section – Priority 2, actions 2.8-2.10.* Many of the measures brought in due to COVID-19, such as the increased use of technology and virtual appointments, will be beneficial for the rare diseases community in the long-term but we must also learn where we can do better. There will be opportunities to learn from COVID-19 and ensure that the experiences of the rare disease community feed into the implementation of the priorities in this new framework and wider national responses to infectious disease outbreaks. Also, it is important to raise awareness about rare diseases by improving the collection of data and making available data for healthcare planning. This includes the expansion and continued support for CARIS to develop and record adult registry data. RDIG will continue work going forward with the other UK nations to develop an information hub to share across the rare diseases community.
Orphan medicines	*See 'Implementation action(s), lead(s) and key performance indicator(s)' section – Priority 4.* In February 2021, the Cross-Party Group published a report with a number of recommendations that should be considered in the development of a Welsh plan: 3. Access to orphan and ultra-orphan medicines **Priority 4 Improving access to specialist care, treatment, and medicines.** **Background** Access to orphan and ultra-orphan medicines are important. The UK should aim to make rare disease medicines available in the NHS as close to receipt of market authorisation as possible where there is a clear unmet clinical need, and the medicine provides (added) value to the NHS in association with an appropriate commercial agreement. Consideration of real-world NHS Wales evidence collated during a potential period of managed access could be used to inform a pre agreed Health Technology Assessment (HTA). Horizon scanning for new drugs for patients in Wales is important to ensure timely awareness of new products and availability of new medicines. The team at All Wales Therapeutics and Toxicology Centre (AWTTC) gathers information about new medicines, indications and formulations that are in development and are expected to be licensed and made available in the UK in the next financial year. They also collect information about Advanced Therapy Medicinal Products (ATMPs) in development that may become available in the next three to five years. This supports the planning, introduction and faster adoption of new medicines in NHS Wales, particularly those that may have significant cost or service planning implications. The horizon scanning team use several sources to collect information about new medicines being developed including the UK-wide horizon scanning database UK PharmaScan. This is the horizon scanning team's primary source of information about new medicines, indications and formulations in development. There is still a place for good clinical engagement and involvement by clinicians. RDIG needs to ensure proper awareness of the horizon scanning functions and support for clinicians. Recognition of the availability and use of new medicines, including consideration of medicines for rare cancers, needs to be made freely available and this will be helped by the introduction of new technologies including Blueteq. This is a high-cost drug management system

	which requires a form to be completed by a doctor for any patient who is prescribed a high-cost drug. This has many benefits including improved speed of access to drugs for patients.
Rare disease research	*See 'Implementation action(s), lead(s) and key performance indicator(s)' section – Actions 1.4, 1.5 and 2.8.*
Alignment beyond the healthcare sector	Much more still needs to be done. Areas such as mental health and the wider importance of support following a diagnosis by agencies wider than healthcare including social care and the third sector are being properly recognised and will need action. There is a need to ensure wide representation of views from across the patient community. Previous successful areas of work along with new initiatives need to be taken forward at pace with appropriate resourcing. Sometimes that will require new funding and business cases. It is important also to remember that much can be achieved without additional resource through new innovative practice and collaboration between various stakeholders. Throughout development of the plan, we have held a number of stakeholder events and joint working with Genetic Alliance UK and Wales Gene Park to try and ensure a wide range of views and ideas about what should be included in the plan are captured. An important principle in those discussions was to consider the available published literature such as the CONCORD study. Rare disease patients and their families can face a lifetime of complex care and living with a rare disease can also have a huge impact on someone's education, financial stability, mobility, and mental health. It is vitally important that the voice of rare disease patients is included when developing wider health and social care policy. People living with rare conditions have been placed under immense pressure by the COVID-19 pandemic. Access to appropriate support, information, care, and treatments has become more difficult and levels of social isolation have increased. Services have been disrupted and it is unclear when reintroduction of some services will resume. Access to personal protective equipment has been challenging, and there has been inflexibility in the education system to respond to individual needs and to adapt practices for children with rare conditions.
Any additional information (for example, background to the strategy or strategy development)	Development of the UK Rare Diseases Framework was based on the outcomes of the 'National conversation on rare diseases', which took place in 2019. The conversation gathered views across the rare disease community on the major challenges faced by people affected by rare conditions across the UK. This included over 230 responses from Wales which have been used to inform the development of this plan. The top issues highlighted by rare disease patients and their families were getting the right diagnosis, access to specialist medical care, awareness amongst health professionals and getting the right support. In addition, in November 2021, two consultation workshops were organised and coordinated by Genetic Alliance UK and the RDIG Chair, Dr Graham Shortland. The aim of the workshops was to engage people affected by rare and genetic conditions in Wales and involve them in the initial phase of the development of a Welsh Action Plan, to implement the Framework. Both sessions were held virtually via Zoom, engaging more than fifty people affected by or representing those affected by rare, genetic, and undiagnosed conditions across Wales. This report details a series of recommendations in relation to the four priority areas of the UK Rare Diseases Framework, based on data collected from the workshops. The underpinning themes of the Framework must be incorporated across each priority area of the Welsh Action Plan and are also addressed separately.

	In addition to the workshops, throughout 2019-2021, the Welsh Cross-Party Group on Rare, Genetic and Undiagnosed Conditions held meetings to discuss priorities for people affected by rare conditions in Wales. In February 2021, the Cross-Party Group published a report with a number of recommendations that should be considered in the development of a Welsh plan: 1. The Welsh Action Plan must include commitments to improve mental health planning and service provision for those affected by rare conditions 2. Transition services must be more flexible when defining the age of transition and supporting individuals holistically with all elements of their care - lack of a diagnosis should not be a barrier to accessing services 3. Access to orphan and ultra-orphan medicines 4. Impact of Covid-19 - data should be collected by Welsh Government that will enable assessment of the impact in terms of morbidity and mortality on people living with rare conditions. During 2021, the Patient Empowerment Group (PEG), a group of patient advocates supporting people affected by rare conditions across the UK coordinated by Genetic Alliance UK produced a report in response to the UK Framework. The report details recommendations to inform the development of action plans across the four priority areas and underpinning themes.

Key: ATMPs: Advanced Therapy Medicinal Products; AWGL: All Wales Genomics Laboratory; AWMGS: All Wales Medical Genomics Service; AWTTC: All Wales Therapeutics and Toxicology Centre; CA: Congenital Anomalies; CARDIS: Congenital Anomaly Register and Information Service; CES: Clinical Exome Sequencing; GPW: Genomics Partnership Wales; HSST: Higher Specialist Scientist Training; ID: Intellectual Disability; MDT: Multi-disciplinary Team; M4RD: Medics 4 Rare Diseases; NCF: National Clinical Framework; NIPT: Non-invasive Prenatal Testing; NSL: Newborn Screening Laboratory; PAG: Patient Advocacy Group; PEG: Patient Empowerment Group; PHW: Public Health Wales; PREM: Patient Reported Experience Measures; PROM: Patient Reported Outcome Measures; RDIG: Rare Diseases Implementation Group; RDNN: Rare Diseases Nurses Network; SNP: Single Nucleotide Polymorphism; STP: Scientist Training Programme; SWAN: Syndrome Without a Name; UHB: University Health Board; WSC: Wales Screening Committee; WES: Whole Exome Sequencing; WG: Welsh Government; WGP: Wales Gene Park; WGS: Whole Genome Sequencing; WHSCC: Welsh Health Specialist Services Committee; WINGS: Wales Infants and Children's Genome Service; WSL: Welsh Screening Laboratory.

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