Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Methods for Generic Justification of New Practices in Ionising Radiation

2 February 2023

Safer Better Care

About the Health Information and Quality Authority

The Health Information and Quality Authority (HIQA) is an independent statutory authority established to promote safety and quality in the provision of health and social care services for the benefit of the health and welfare of the public.

HIQA's mandate to date extends across a wide range of public, private and voluntary sector services. Reporting to the Minister for Health and engaging with the Minister for Children, Equality, Disability, Integration and Youth, HIQA has responsibility for the following:

- **Setting standards for health and social care services** — Developing person-centred standards and guidance, based on evidence and international best practice, for health and social care services in Ireland.
- **Regulating social care services** — The Chief Inspector within HIQA is responsible for registering and inspecting residential services for older people and people with a disability, and children's special care units.
- **Regulating health services —** Regulating medical exposure to ionising radiation.
- **Monitoring services** — Monitoring the safety and quality of health services and children's social services, and investigating as necessary serious concerns about the health and welfare of people who use these services.
- **Health technology assessment** — Evaluating the clinical and cost-effectiveness of health programmes, policies, medicines, medical equipment, diagnostic and surgical techniques, health promotion and protection activities, and providing advice to enable the best use of resources and the best outcomes for people who use our health service.
- **Health information** — Advising on the efficient and secure collection and sharing of health information, setting standards, evaluating information resources and publishing information on the delivery and performance of Ireland's health and social care services.
- **National Care Experience Programme** — Carrying out national service-user experience surveys across a range of health services, in conjunction with the Department of Health and the HSE.

Foreword

Ionising radiation is increasingly being used in both the diagnosis and treatment of disease, and innovations in this area have the potential to improve the health and well-being of patients. The risks to a person receiving a medical exposure to ionising radiation are generally low. However, all medical exposures to ionising radiation carry some risk.

The European Union Basic Safety Standards for the Protection Against Dangers from Medical Exposure to Ionising Radiation (Euratom) were initially transposed into Irish law under SI 256 in January 2019. These Regulations named HIQA as the Competent Authority for medical exposure to ionising radiation. One requirement under the Regulations is that new practices involving medical exposure must be justified by HIQA before they are generally adopted – this is known as generic justification.

This methods document sets out how HIQA will carry out generic justification of new practices and provides guidance to applicants seeking generic justification.

Work on this methods document was undertaken by the Ionising Radiation Evidence Review Team from the HTA Directorate in HIQA. A multidisciplinary Medical Exposure to Ionising Radiation Expert Advisory Group, convened by HIQA to support its work in this area, advised on the preparation of this document. HIQA would like to thank the Evidence Review Team, the members of the Expert Advisory Group and all who contributed to the preparation of this document.

Dr Máirín Ryan

Director of Health Technology Assessment & Deputy CEO

Health Information and Quality Authority

Contents

Acknowledgements

HIQA would like to thank all of the individuals and organisations who provided their time, advice and information in support of this methodology document.

Particular thanks are due to the Medical Exposure to Ionising Radiation (MEIR) Expert Advisory Group (EAG) and the individuals within the organisations listed below who provided advice and information.

The membership of the MEIR EAG is as follows:

Prof Mary Coffey, Chairperson	Independent Chairperson
Dr Jennie Cooke	Irish Association of Physicists in Medicine, *Principal Physicist (Diagnostic Radiology), Children's Health Ireland*
To be confirmed	HSE National Heart Programme *Consultant Cardiologist*
Dr Agnella Craig	HIQA Healthcare Directorate, *Regional Manager, Ionising Radiation Regulation Team, HIQA*
Prof Clare Faul	HSE National Cancer Control Programme, *Consultant Radiation Oncologist*
Dr Eva Godske Friberg	International Expert, *Senior Medical Application Advisor, Department of Radiation and Environmental Safety Section for Medical Appliances, Norwegian Radiation and Nuclear Safety Authority*
Ms Patricia Heckman	HSE National Cancer Control Programme, *Chief Pharmacist & NCCP lead on radionuclides licensed as medicines*
Ms Geraldine Jolley	SAGE Advocacy, *Patient Advocate*
Dr Peter Kavanagh	HSE National Clinical Programme for Radiology and Faculty of Radiologists, Royal College of Surgeons in Ireland *Consultant Radiologist*

Mr Aodh MacGairbhith	Irish Association of Physicists in Medicine, *Medical Physicist (Radiation Oncology)*
Ms Michele Monahan	Irish Institute of Radiography and Radiation Therapists (Diagnostic Radiography), *Radiography Services Manager*
Ms Emer Lahiff	Health Products Regulatory Authority, Technology Group Lead, Assessment & Surveillance, Medical Devices
Ms Collette O'Connor	Environmental Protection Agency, *Senior Inspector*
Dr Maria O'Grady	Irish Dental Association, *Dentist*
Ms Edel O'Toole	Irish Institute of Radiography and Radiation Therapists (Radiation Therapy), *Radiation Safety Officer/Radiation Protection Officer*
Mr Niall Phelan	National Screening Service, HSE, *Chief Physicist, BreastCheck*
Prof Susan Smith	Methodology Expert, *Professor of General Practice, Public Health and Primary Care*
To be confirmed	Patients for Patient Safety, *Patient Representative*
To be confirmed	Irish Nuclear Medicine Association *Consultant Radiologist*

Thanks are due to the Expert Advisory Group (EAG) of 2019-2020 who provided advice and information:

Mr Steve Ebdon-Jackson, Dr John Feeney, Dr Aileen Flavin, Dr Shane Foley, Mr Dean Harper, Dr Peter Kavanagh, Prof Jim Malone, Dr Ronan Margey, Dr Joseph Martin, Ms Margaret Moore, Dr Robert O'Connor, Dr Geraldine O'Reilly, Mr Niall Phelan, Mr David Pollard, Dr Jane Renehan, Prof Susan Smith, Ms Anne Tobin, Ms Gerarda Warnes, Ms Janet Wynne.

Organisations that assisted the Authority in providing information, in writing or through meetings, included:

Private Hospitals Association, the Irish Cancer Society and the Irish Cardiac Society.

Members of the Ionising Radiation Evidence Review Team:

Members of HIQA's Ionising Radiation Evidence Review Team are Dr Paula Byrne*, Ms Marie Carrigan, Mr Andrew Dullea, Dr Patricia Harrington, Ms Maeve McGarry, Dr Kirsty O'Brien, Dr Lydia O'Sullivan, Dr Susan Spillane.

Conflicts of Interest

None reported.

* Left HIQA in March 2022.

List of Abbreviations

AGREE II	'Appraisal of Guidelines for Research & Evaluation' instrument
AMSTAR-2	'A MeaSurement Tool to Assess systematic Reviews' instrument
BED	biologically effective dose
BSS	Basic Safety Standards
EAG	expert advisory group
ERT	evidence review team
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
HIQA	Health Information and Quality Authority
HSE	Health Services Executive
HTA	health technology assessment
IR	ionising radiation
MEIR	medical exposure to ionising radiation
PICO	Population, Intervention, Comparator, Outcome
QUADAS-2	'Quality Assessment of Diagnostic Accuracy Studies' tool
RCT	randomised controlled trial
RQ	research question
SI	Statutory Instrument
SoF	Summary of findings

1 Background

Ionising radiation is used in both the diagnosis and treatment of disease. While the risks are generally considered to be low, all medical exposures to ionising radiation carry some risk. One of the main risks associated with medical exposure to ionising radiation is the increased risk of developing cancer – this risk may persist for decades. The key principles of radiation protection are justification, optimisation and dose limitation – these form the basis of European and Irish legislation, which aim to protect members of the public from the dangers of medical exposure to ionising radiation.[1-4]

The European Council Directive 2013/59/Euratom Basic Safety Standards for Protection Against Dangers Arising from Medical Exposure to Ionising Radiation sets out basic safety standards which apply to medical exposure ('The Directive').[1] The Directive was transposed into Irish law in 2019 as the European Union (Basic Safety Standards for Protection against Dangers Arising from Medical Exposure to Ionising Radiation) Regulations 2018 (SI 256/2018).[2] These regulations have been subject to amendment under SI 332/2019 [3] and SI 413/2019 [4] and are referred to together in this document as "the Regulations". The Regulations designate HIQA as the Competent Authority in Ireland for the regulation of medical exposure to ionising radiation.

1.1 What is justification?

Justification is a process of demonstrating that there is a sufficient net benefit associated with a radiation exposure.[5, 6] This takes into account the efficacy and potential benefits of the exposure, the possible risks associated with the exposure, and any alternatives which may be available.

The Directive [1] explains justification as outlined in Table 1.

Table 1: Explanations of Justification according to 2013/59/Euratom

Article 5 (General Principles of Radiation Protection)
Justification: Decisions introducing a practice shall be justified in the sense that such decisions shall be taken with the intent to ensure that the **individual or societal benefit** resulting from the practice **outweighs the health detriment** that it may cause. Decisions introducing or altering an exposure pathway for existing and emergency exposure situations shall be justified in the sense that they should do more good than harm.

Article 55 (Justification)
Medical exposure shall show a **sufficient net benefit**, weighing the total potential diagnostic or therapeutic benefits it produces, including the direct benefits to the health of an **individual** and the benefits to **society**, against the individual **detriment** that the exposure might cause, taking into account the efficacy, benefits and risks of **available alternative techniques** having the same objective but involving **no or less exposure** to ionising radiation.

Table 2 outlines the three levels of justification of a radiological practice recognised internationally.[5, 6]

Table 2: Levels of justification of radiological practices

Level	Consideration
1	**Considers the use of radiation in medicine in general.** The proper use of radiation in medicine is accepted as doing more good than harm to society, since, in general, the net benefits outweigh the harms. General level of justification is now taken for granted.
2	**Undertaken at a population level for a type of practice.** Level 2 justification considers whether, in general, for a specified practice with a specified objective, the benefits outweigh the risks. At a population level, the practice should be judged to usually improve the diagnosis or treatment, or to provide necessary information about the exposed individuals. For example, chest X-rays for patients showing relevant symptoms, or a group of individuals at risk for a condition that can be detected and treated).
3	**Considers the diagnostic or therapeutic outcome at an individual patient level.** This is assigned to the healthcare professionals involved in the patient's care. All individual medical exposures should be justified in advance, taking into account the specific objectives of the exposure and the characteristics of the individual involved. That is, the particular application should be judged to provide more good than harm for the individual patient.

Source: International Commission on Radiological Protection [5, 6]

Level 2 justification can be referred to as '**generic justification**' of practices, or practices that are 'justified in general'. Under the Regulations, HIQA is the

Competent Authority for justification of practices prior to them becoming generally adopted.[†] Furthermore, under the Regulations, HIQA may review the generic justification of an existing practice if new and important evidence about the practice emerges, or if new and important evidence about other techniques and technologies (including non-ionising practices) emerges.[‡]

The process of generic justification is undertaken at a population level and considers the potential benefits and harms associated with medical exposure to ionising radiation. The decision to justify a new practice must also take into consideration the effectiveness, advantages and risks associated with alternative practices which expose the individual to less or no ionising radiation. In addition, the Regulations specifically call out the need to assess public and occupational exposure in the course of justification.[§] If a practice has been generically justified, the individual exposure must still be justified (that is, Level 3 justification) and practitioners should choose the most appropriate course of action that meets the needs of the individual.

In exceptional circumstances (for example, compassionate use, Regulation 8(9) of SI 256 allows for individual patient access to practices which are not justified by HIQA; however, it is the responsibility of the undertaking to ensure that the specific individual exposure is justified.[**] The undertaking should be aware that this provision can only be used where appropriate and in special circumstances. Such an exposure should be evaluated on a case-by-case basis and the details of the exposure and its justification should be well documented. This provision cannot be used to introduce new practices for general use that have not yet been justified by HIQA. Regulation 8(9) applies in conjunction with any relevant requirements within the regulatory framework for medical devices and medicinal products (for example, compassionate use programmes for medical devices).

Generic justification does not apply to new practices that are being offered solely in the context of a clinical trial, clinical investigation or research study. In Ireland, such research comes under the governance of the relevant clinical trial(7) and clinical investigation legislation(8), the Health Products Regulatory Authority and research ethics committees.(9)

Having market authorisation for a medicinal product (or CE marking in the case of a medical device) does not circumvent the requirements of the Regulations. Similarly,

[†] Regulation 7(1) of SI 256 2018.
[‡] Regulation 7(3) of SI 256 2018.
[§] Regulation 7(6) of SI 256 2018.
[**] Clarification on the definition of an undertaking is given in a HIQA Regulation Notice from 2019. Undertakings should not be confused with practitioners.

regulatory derogations or exemptions allowing market access do not circumvent the requirements of the Regulations.

1.2 What is a new practice?

A 'new' practice is defined as a class or type of radiological procedure which was not used prior to the introduction of the Regulations, that is, before 8 January 2019.[††]

The term 'class or type of practice' refers broadly to both the technology (that is, the radiopharmaceutical, device or technique) and the objective to be achieved by using that technology, that is, the clinical indication. The Directive does not provide a definition of a type or class of practice and for this reason, member states differ in how they define new 'classes or types of practice'. In the Irish context, a new class or type of practice will **typically** mean:

- new technologies (that is, sealed or unsealed sources, a radiopharmaceutical, device or technique)
- use of an existing technology for a new indication (that is, a new clinical condition(s) or anatomical region(s) under investigation or treatment)
- new combinations of existing technologies for a specific indication (for example, mammography plus tomosynthesis for breast cancer screening)
- new intended populations (for example, change from an adult to a paediatric population, or from a symptomatic to an asymptomatic population)
- in radiation oncology: a new indication, site or population for hypo- or hyperfractionation.

Also, radiological procedures to be used as part of health screening programmes require generic justification prior to the commencement of such programmes in accordance with Regulation 8(3).

In general, dose optimisation is a separate concept under 59/2013/Euratom and does not represent a new class or type of practice. For example, in diagnostic imaging or imaging for planning, intervention, guiding and verification purposes, changes to scanning parameters using the same scanning technique and device for the same clinical objective would not require generic justification. In radiation oncology, changes to beam orientation using the same radiotherapy technique and device would be considered optimisation and would not require generic justification. Also, in radiation oncology, radiobiological compensation for missed treatments (for

[††] Regulation 2(1) of SI 256 2018

example, by providing bi-daily treatments or by changing the dose per remaining treatments) would not require generic justification as this should be justified on an individual patient basis. While significant changes to fractionation schedules at a population level may need to be generically justified, optimisation of individual patient treatment plans resulting in variation in fractionation would not require generic justification.

Radiological practices are quite broad, and there may be other practices which do not clearly fall under the examples above, yet require generic justification. If you are uncertain whether a particular practice requires generic justification, queries can be sent to radiationjustification@hiqa.ie.

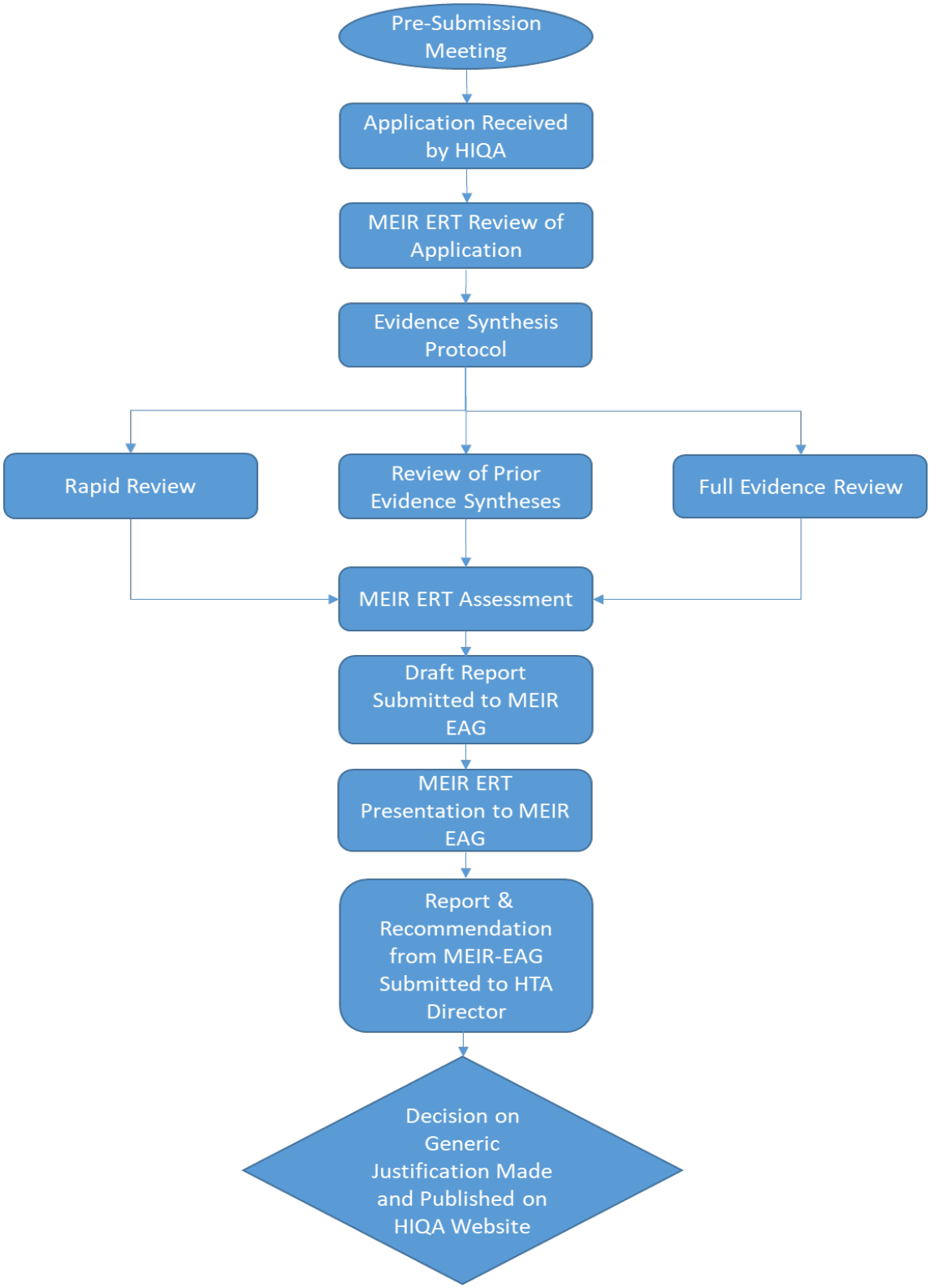
2 HIQA's Approach to Generic Justification

The Regulations provide the legal framework on which the principles of justification and optimisation are applied by HIQA, helping safeguard each service user along their pathway of diagnosis or treatment involving ionising radiation. The purpose of this guidance is to provide information and guidance on HIQA's processes for those seeking to apply to HIQA for generic justification of new types of practices involving medical exposure. This methods document provides guidance only and it is recommended that it should be used in conjunction with the Directive and the Regulations, with the latter taking precedence.

HIQA's approach to generic justification involves a system whereby assessment and decision-making for generic justification are separated. The process is supported by HIQA's Medical Exposure to Ionising Radiation (MEIR) Evidence Review Team (ERT) and an Expert Advisory Group (EAG) comprising key stakeholders (See Section 3). The assessment process to inform the justification of a new class or type of practice will involve review and appraisal of scientific literature (See Section 4). For each type of practice under consideration, the HIQA ERT will prepare a report summarising the assessment process and the findings. Evidence-informed decision making is then further enabled by the use of a framework with specific criteria and judgments that cover the basis for justification (See Section 5). The report, associated evidence and judgments used to inform justification will be submitted to the EAG for review and feedback. The Chairperson of the EAG will make a formal submission to the Director of Health Technology Assessment (HTA) outlining the group's recommendation. The Director of HTA will then make the decision on behalf of HIQA on whether the new MEIR practice should be generically justified or not. The process by which decisions will be made and the information disseminated is outlined in Section 6.

A simplified and condensed overview of HIQA's approach to generic justification is provided in Figure 1. Each of the steps are described in detail in the subsequent sections.

Figure 1: Simplified Schematic of the Generic Justification Process



HIQA is also identified as a competent authority under the Regulations for implementing a system of inspection and enforcement (the regulatory framework) to ensure that action is taken to remedy any deficiencies identified through inspection and to prevent their recurrence. As part of this regulatory framework, HIQA is responsible for ensuring that public and private facilities in Ireland providing medical and dental radiological services to people are compliant with the Regulations. The regulations include a suite of enforcement tools available to HIQA in the event of non-compliance with the Regulations. For further information on HIQA's regulatory framework for medical exposure to ionising radiation, please refer to the Guidance on the Assessment of Compliance in Undertakings Providing Medical Exposure to Ionising Radiation [(10)] and the Assessment Judgement Framework for Ionising Radiation[(11)] or email radiationprotection@hiqa.ie.

3 Evidence Review Team and Expert Advisory Group

3.1 MEIR Evidence Review Team

The ERT comprises members of HIQA's HTA Directorate. A lead researcher (project lead) will be assigned for each application for generic justification. The HIQA ERT will review the application and prepare a written report for the proposed new practice which will be sent to the EAG and the Director of HTA.

3.2 MEIR Expert Advisory Group

HIQA has convened a standing EAG to support its work. The EAG comprises an independently appointed chairperson and nominations from key stakeholder groups with various expertise to help contextualise evidence and provide insights into a broad variety of generic justification applications. The role of the EAG is to review the draft report and draft judgements prepared by the HIQA ERT and advise on the content and the interpretation of the evidence. The EAG will provide recommendations on the justification of new practices to the Director of HTA, who will make the final decision on behalf of HIQA. The membership and terms of reference for the EAG are published on the HIQA website. The chairperson is responsible for ensuring the required mix of expertise is present in advance of any specific discussions or presentations on generic justification applications and will facilitate the formation of EAG recommendations and advice as needed.

The EAG will meet three times a year, typically in February, June, and October. Dates of the EAG meetings will be published on the HIQA website.

3.3 Conflicts of interest

Conflicts of interests will be considered when the EAG is formed and following the nomination of any new members. All members of the HIQA ERT and EAG will be required to submit annual declarations of interest. In addition, because potential conflicts of interest can vary across topics, members will be invited to make a declaration in the context of the specific topics under consideration prior to each meeting.

The HIQA conflict of interest policy and standard operating procedure specify actions to address any conflicts declared, ranging from simply declaring a conflict of interest to excluding EAG members from discussions of specific topics. Where a conflict of interest specific to a given generic justification application exists, there may be an option for the nominating body to suggest an alternate nominee. As needed, adjudication of declared actual or perceived conflicts will be undertaken by the Chairperson of the EAG in collaboration with the Director of HTA.

4 Applications and Evidence Synthesis

4.1 Applying to HIQA

To initiate the application process for generic justification, an application form (Appendix I) must be completed and submitted to HIQA. Potential applicants are strongly encouraged to engage with the HIQA ERT prior to submitting an application. HIQA will consider the application form and any other information or submissions provided by applicants during the application process. HIQA will also provide periodic updates to the applicant during the generic justification process.

The following are examples of professionals and bodies that may be best placed to complete an application and provide the required information. However, input from more than one of the below will likely help provide the most complete application form possible:

- Representatives from National Clinical Programmes
- Representatives of an Undertaking
- Radiation Therapy Services Managers
- Radiography Services Managers
- Chief or Principal Medical Physicists
- Consultant Radiologists

- Consultant Radiation Oncologists.

The HIQA ERT will work to support applications using the available resources at their disposal. To build capacity within the healthcare system, a two-phased approach will be used to roll out a national system for generic justification. During the initial roll-out phase, the HIQA ERT will endeavour to work closely with applicants and to provide additional support in the preparation of the evidence synthesis report where possible. This will allow the potential applicants to become acquainted with HIQA's approach and to help undertakings when planning the introduction of new practices. However, prospective applicants can also independently conduct the requisite evidence synthesis necessary to support their application. After the initial roll-out phase, to ensure sustainability, applicants will be expected to complete the evidence synthesis report and submit it to the HIQA ERT for review and appraisal. HIQA will work with stakeholders in the roll-out phase to increase awareness and knowledge of expectations around evidence synthesis in generic justification. This initial roll-out phase of the generic justification process will end in June 2024.

4.2 Pre-Submission Meeting

Potential applicants are strongly encouraged to discuss their proposed generic justification with the HIQA ERT prior to submitting an application. The HIQA ERT will endeavour to arrange a pre-submission meeting to discuss potential applications, answer queries, provide guidance on HIQA's process for receipt and consideration of applications for generic justification, assist applicants in identifying whether generic justification is required, and help ensure the requisite information is provided in the application form.

4.3 Applications and MEIR ERT Review

Following receipt of the application, the HIQA ERT will work to review the completed application form and provide direction on the required methodology. The type of review required will be determined by the HIQA ERT based on the information contained in the application form and preliminary scoping of the topic. One of these three types of reviews will generally be undertaken:

- Rapid Review
- Review of Prior Evidence Syntheses
- Full Evidence Review (Systematic Review).

These review types are described in detail in Section 4.5. The following matrix, in conjunction with the information provided in the application form will guide the HIQA ERT in determining the appropriate review methodology (Figure 2). The matrix

focusses on two factors: the level of risk associated with the practice and how established the practice is elsewhere (for example, if it has been generically justified in another country).

Figure 2: Evidence Synthesis Matrix for Generic Justification

	Dose significantly increased compared with current practice	Existing technology/methodology, but focus is a different anatomical region and there is no significant increase in dose	Practice decreases dose compared with current practice and *decreases* the diagnostic performance or clinical benefit of the practice	Changes to fractionation schedules at population level (e.g. hypo- or hyperfractionation)	Practice decreases dose compared with current practice but *does not decrease* the diagnostic performance or clinical benefit of the practice	Number or type of sources of radiation has changed, but there is no significant increase in dose
Completely new practice	Full Evidence Review	Full Evidence Review	Full Evidence Review	Full Evidence Review	Full Evidence Review	Full Evidence Review
New practice to Ireland, but is undertaken elsewhere with limited evidence available	Full Evidence Review	Full Evidence Review	Full Evidence Review	Review of Prior Evidence Syntheses	Rapid Review	Rapid Review
New practice to Ireland, but is undertaken elsewhere (EU or non EU), or generically justified by another EU country, with a good availability of evidence	Review of Prior Evidence Syntheses	Review of Prior Evidence Syntheses	Review of Prior Evidence Syntheses	Rapid Review	Rapid Review	Rapid Review

This matrix is provided for guidance purposes and should be read in the context of the typical example of a new type or class of practice, as outlined in this document. Please consult HIQA if the practice does not fit the description of any of the categories described.

In some circumstances, based on initial findings or preliminary searches, the HIQA ERT may determine that a different review methodology is required to that outlined in the matrix and will inform the applicant of same.

4.4 Evidence Synthesis Protocol

The following section outlines the general approach to devising a protocol. The protocol should be submitted to the HIQA ERT in advance of conducting the evidence synthesis or systematic search. The HIQA ERT review may help identify issues early on and prevent delays in the generic justification process.

An initial topic exploration exercise may help establish the extent, type and quality of evidence available, the relevant comparators (and/or reference standards), outcomes and the quality assessment tools which should be applied.

If required to undertake a full systematic review of the literature, it is suggested that this section is read in conjunction with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P).[12] If required to conduct a rapid review or appraisal of reviews and international guidelines, it is reasonable to omit some of the points specified in PRISMA-P.

The evidence synthesis protocol will identify the criteria against which the practice will be assessed, formulate the review question, select the appropriate inclusion and exclusion criteria, and identify the range of relevant sources and the relevant outcomes. These steps are described in the following sections.

a) Formulate the research question(s)

The first step in evidence synthesis is to clearly formulate the research questions (RQ)s using a structured format, such as the 'Population Intervention Comparator, Outcome' (PICO).[13] An appropriate patient population should be defined in light of the RQ, stating key factors that could affect test or intervention effects such as setting, disease severity and prevalence, and prior testing.[14] If there is more than one RQ, the PICO should be defined for each question.

b) Establish the inclusion and exclusion criteria

The type of studies that will be included in the review will be pre-specified and will be informed by the scoping exercise. Consideration should be given to the hierarchy of the available evidence;[15] for example, it may be the case that high-quality randomised controlled trials (RCTs) are not available to answer the RQs. The inclusion and exclusion criteria should be designed so that only relevant studies which are within scope and can answer the research question are included. The pre-

specified eligibility criteria for inclusion of studies should be based on study characteristics such as the PICO, study design, setting and time frame, and report characteristics such as the years considered, language and publication status.

c) Select outcomes and rate their importance

Patient-relevant outcomes should be initially selected as part of the evidence synthesis protocol. These outcomes should be relevant to clinical effectiveness and safety. Where surrogate endpoints are chosen, the rationale for their use must be documented. The surrogate endpoints must have a clear biological or medical rationale for their use or have a strong and validated link to a final endpoint. With respect to safety, outcomes selected should include adverse effects of clinical importance with particular attention given to those that differ substantively between the proposed practice and the comparator. Consideration should be given to potential harms that are short-term and those of lasting effect, and the potential for both the severity and frequency of these harms.

d) Select relevant quality assessment tools

Not all studies or reviews may be of the same quality; published peer-reviewed literature may be subject to bias. It is therefore necessary to assess and document the quality of the included studies as part of evidence synthesis.

Practices involving MEIR range across a broad spectrum of diagnostic and therapeutic specialities. The appropriate quality assessment tool is likely to vary depending on the practice being considered for generic justification, the type of studies included and emerging methods of quality assessment. For example, QUADAS-2, is a tool frequently used in systematic reviews to evaluate the risk of bias and applicability of individual diagnostic accuracy studies.[16] For appraisals of published systematic reviews and international guidelines, the instruments AMSTAR-2[17] and AGREE II[18] or AGREE GRS[19] should be referred to as an initial starting point. It is strongly suggested that applicants refer also to the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) framework, which includes a widely adopted tool for grading the quality of a body of evidence as a whole.[20]

4.5 Evidence Synthesis Methodologies

The methods used for each of the three types of review of a new practice are described in this section. Advice on the type of review that should be undertaken will be provided by the HIQA ERT after an application is submitted with feedback provided to the applicant. The findings from the reviews completed in accordance

with one of the methodologies outlined in this section will be incorporated into an 'Evidence Profile' which will be used by the HIQA ERT in their report to the EAG and the Director of HTA (see Section 5).

4.5.1 Rapid Review

In many circumstances, if, relative to current practice, the proposed new practice does not exceed the current dose of ionising radiation (including the biological effective dose (BED), where applicable) and there are no additional safety issues identified, a rapid review shall be sufficient.

Rapid reviews allow for more timely evidence synthesis compared to standard systematic reviews at the expense of being slightly less robust. They are therefore used only where the proposed practice is well established elsewhere and the proposed new practice presents a similar, limited risk to the current practice. Additional guidance in the conduct of rapid reviews, including recommendations with regard to searching, study selection, data extraction, risk of bias assessment, evidence synthesis and grading the certainty of the evidence, is available from the Cochrane Rapid Reviews Methods Group.[21]

4.5.2 Review of Prior Evidence Synthesis

Applications which are suitable for review of prior evidence syntheses will usually comprise practices which are new to Ireland, but are well established in other countries and have a strong evidence base. The evidence synthesis to support generic justification in Ireland may be available from these countries and the applicant can submit this to the HIQA ERT when submitting their application form. This may take the form of generic justification reports from other agencies, health technology assessments, guidelines or systematic reviews.

Methodologies used in the appraisal of reviews and international guidelines are underpinned by the availability of high quality, relevant systematic review(s) or clinical guidelines which will ensure efficient processing of an application for justification. The quality of systematic reviews and guidelines can vary greatly and therefore quality needs to be formally appraised and documented. Available tools include AMSTAR II[17] and ROBIS[22] (for systematic reviews), and AGREE II[18] or AGREE GRS (clinical guidelines).[19] Evidence that has not already been systematically reviewed or which is not considered relevant or of sufficient quality may have to undergo a full evidence review as described in Section 4.5.3.

4.5.3 Full Evidence Review

If a full evidence review is required, a systematic review of the literature should be undertaken; this may entail an update of an existing systematic review, if appropriate. The method for undertaking a systematic review should be in line with international best practice, for example, according to Cochrane methodology.[23] The methods used to analyse or combine data should be clearly outlined and justified, and the data provided in both aggregated and disaggregated form. Meta-analysis may be used to synthesise outcome data, provided there are sufficient, relevant and valid data to justify this approach. A risk of bias assessment using a recognised method (for example, the Cochrane risk of bias tool) should be presented. If the data limits the use of a quantitative summary, a qualitative summary may be provided. The characteristics and limitations of the study data included in the analysis should be clearly documented.

Summary of findings (SoF) tables should be developed. These present the key findings from a systematic review, specifically the most important outcomes (both benefits and harms), the size of these effects, and the certainty of this evidence. Guidance on the preparation of SoF tables is available from the Cochrane Collaboration.[20] Software such as the GRADE's GRADEpro GDT software - https://www.gradepro.org/ can be used to produce the tables.

5 Moving from Evidence to a Decision

HIQA's approach when moving from the evidence to a generic justification decision is based on a modified version of the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) Evidence to Decision (EtD) framework, which was developed to facilitate systematic and transparent decision-making.[24] HIQA has identified key criteria in line with the general principles set out for justification in the Directive which will support HIQA to move from the evidence to a decision.

1. Benefits
2. Test Accuracy
3. Risks (Detriments)
4. Importance of Outcomes
5. Balance of Benefits & Risks.

Not all criteria will be applicable (for example, test accuracy) to every practice being considered for generic justification. For each of the relevant criteria, the evidence will be considered in terms of the specific outcomes considered, the magnitude of the effects and the overall certainty of the evidence. Where relevant, additional

considerations in relation to the applicability of the evidence will also be documented by the HIQA ERT.

Draft judgements against the criteria will be completed by the HIQA ERT, and brought to the EAG who will independently review the judgements, offer suggestions and help support contextualisation of the evidence (see Section 5.1). Outputs from the EtD framework will inform decisions, and may help identify caveats, advice or additional considerations that will accompany the decision.

5.1 Presentation to MEIR Expert Advisory Group

The HIQA ERT will submit a draft summary report outlining the review's key findings and any other relevant information to the EAG. These documents will be supplemented by an oral presentation by the HIQA ERT at the EAG meeting. Following the clarification of any questions regarding the evidence, there will be an opportunity for discussion by the EAG regarding potential caveats or additional contextual considerations specific to the generic justification recommendation under consideration. If specific additional considerations need to be addressed, the recommendation may be deferred until the next scheduled meeting of the EAG. Where appropriate, such comments will be addressed by the HIQA ERT.

Following consideration of the evidence, the EAG Chairperson will call for a motion on justification. Ideally, the EAG will come to a consensus on whether a new practice should be generically justified or not. Where relevant, dissenting views and or additional considerations from both the EAG and HIQA ERT will be captured in the final report in line with the EtD framework. The Chair will submit a formal recommendation on behalf of the EAG, to the Director of HTA, including the rationale for same.

5.2 Decisions on Justification

HIQA, the authority under SI 256 2018, retains the statutory responsibility for generic justification. Decisions on the generic justification of a practice will be made by the Director of HTA on behalf of HIQA. Decisions on generic justification are informed by the objective appraisal of the evidence and recommendations from the EAG.

While the evidence synthesis methodology may vary between generic justifications, the criteria, as outlined in Section 5, that are used to assess applications for justification are explicit. HIQA will endeavour to be transparent in its methods, including the choice of methods and the specific criteria considered in each generic justification decision. The HIQA ERT will be transparent regarding what evidence is

used to inform each judgment. Similarly, the recommendation by the EAG will be clearly documented.

As outlined in Figure 1 and Section 5.1, the Chairperson will submit a formal recommendation on behalf of the EAG, to the Director of HTA, including the rationale for same. This submission along with the completed application form, any other relevant information and the final summary report outlining the key findings of the review will form the basis for the decision on the generic justification of the practice by the Director of HTA on behalf of HIQA.

6 Publication of Justification Decision

Once the Director of HTA makes the decision on the generic justification of a practice, a final report will be prepared for publication, and the decision will be posted on the HIQA website. The applicant shall be informed of the decision in advance of publication. Names of the applicant's affiliated institution or organisation will be included in the final publication.

7 Revision of Decision Following Justification

If new and important evidence about the practice is acquired after being generically justified, or if new and important information about alternative techniques and technologies is acquired (including non-ionising practices), a review of a justification decision may be undertaken. This is within HIQA's statutory remit and is provided for under Regulation 7(3).[(2)] Similarly, if new and important evidence on practices involving ionising radiation in existence prior to the implementation of the Regulations emerges, HIQA may review their generic justification.

If a decision is taken that a practice is not justified, this does not preclude the submission of a new application for generic justification if new evidence is identified.

8 Contacting HIQA

As outlined in Section 4, the HIQA ERT will work to support potential applicants with the application process. Queries can be directed to the Evidence Review Team in HIQA via email (radiationjustification@hiqa.ie) or by telephone 01 828 6700.

9 References

1. Council Directive, European Union, 2013/59/EURATOM https://eur-lex.europa.eu/eli/dir/2013/59/oj?msclkid=fc428f7cab5a11ec9716a1db9443e61e (2013).
2. European Union (Basic Safety Standards for Protection Against Dangers Arising from Medical Exposure to Ionising Radiation) Regulations 2018 S.I. No. 256 of 2018. http://www.irishstatutebook.ie/eli/2018/si/256/made/en/print Dublin: The Stationary Office, (2019).
3. European Union (Basic Safety Standards for Protection Against Dangers Arising from Medical Exposure to Ionising Radiation) Regulations 2019 S.I. No. 332 of 2019. https://www.irishstatutebook.ie/eli/2019/si/332/made/en/print Dublin: The Stationary Office, (2019).
4. European Union (Basic Safety Standards for Protection Against Dangers Arising from Medical Exposure to Ionising Radiation) Regulations 2019 S.I. No. 413 of 2019. https://www.irishstatutebook.ie/eli/2019/si/413/made/en/print Dublin: The Stationary Office, (2019).
5. International Commission on Radiological Protection The 2007 Recommendations of the International Commission on Radiological Protection Publication 103. Ann ICRP. 2007;37:1-63.
6. International Commission on Radiological Protection The 2007 Recommendations of the International Commission on Radiological Protection Publication 105. Ann ICRP. 2007;37(2-4).
7. European Union (Clinical Trials on Medicinal Products for Human Use) (Principal) (Amendment) Regulations 2022. Dublin: The Stationary Office., (2022).
8. Medical Devices (Amendment) Regulations 2021. Dublin: The Stationary Office, (2021).
9. European Union (Clinical Trials on Medicinal Products for Human Use) (National Research Ethics Committees) Regulations 2022. Dublin: The Stationary Office, (2022).
10. Health Information and Quality Authority. Guidance on the assessment of compliance in undertakings providing medical exposure to ionising radiation Updated September 2019.
11. Health Information and Quality Authority. Assessment-judgment framework for undertakings providing medical exposure to ionising radiation. Updated Sept 2019.
12. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Annals of internal medicine. 2009;151(4):264-9.

13. Taylor K. Tip for data extraction in meta-analysis – 19 [Internet]. Oxford: Centre for Evidence-Based Medicine. 2019. Available from: https://www.cebm.net/2019/10/tip-for-data-extraction-in-meta-analysis-19/.

14. Reitsma J, Rutjes A, Whiting P, Vlassov V, Leeflang M, Deeks J. Assessing methodological quality. Cochrane handbook for systematic reviews of diagnostic test accuracy version. 2009;1(0).

15. Oxford Centre for Evidence-Based Medicine Levels of Evidence Working Group. The Oxford Levels of Evidence 2. Available from: https://www.cebm.net/index.aspx?o=5653.

16. Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Annals of internal medicine. 2011;155(8):529-36.

17. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. bmj. 2017;358:j4008.

18. Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2010;182(18):E839-42.

19. Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al. The Global Rating Scale complements the AGREE II in advancing the quality of practice guidelines. J Clin Epidemiol. 2012;65(5):526-34.

20. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336(7650):924-6.

21. Garritty C, Gartlehner G, Nussbaumer-Streit B, King VJ, Hamel C, Kamel C, et al. Cochrane Rapid Reviews Methods Group offers evidence-informed guidance to conduct rapid reviews. J Clin Epidemiol. 2021;130:13-22.

22. Whiting P, Savović J, Higgins JP, Caldwell DM, Reeves BC, Shea B, et al. ROBIS: A new tool to assess risk of bias in systematic reviews was developed. J Clin Epidemiol. 2016;69:225-34.

23. Higgins JP, Green S. Cochrane handbook for systematic reviews of interventions: John Wiley & Sons; 2011.

24. Alonso-Coello P, Schünemann HJ, Moberg J, Brignardello-Petersen R, Akl EA, Davoli M, et al. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction. BMJ. 2016;353:i2016.

10 Appendix I Generic Justification Application Form

Please see the HIQA website for the most up to date stand-alone version which may be submitted to HIQA.

Health Information and Quality Authority Application for generic justification	

This form allows you to submit an application for the generic justification of a new type of practice which involves medical exposure to ionising radiation. This form must be used when applying to HIQA.

Applicant details	
Applicant **name** (e.g., organisation, institution)	
Applicant **address** (include **Eircode**)	
Designated point of contact (DPOC) **name**	
DPOC **email address**	
DPOC **contact number**	

Undertaking/Service provider details (e.g., hospital) – if different from the above	
Undertaking **name** (e.g. organisation, institution)	
Undertaking **address** (include **Eircode**)	
Designated point of contact (DPOC) **name**	
DPOC **email address**	
DPOC **contact number**	

Section 1. Details of practice			
Into which of the following **categories** does the practice fit?			
Computed Tomography (CT)	☐	Mammography	☐
Dental	☐	Nuclear medicine	☐
Dual-energy X-ray absorptiometry (DXA)	☐	Positron Emission Tomography/CT	☐
Fluoroscopy	☐	Radiology – general	☐
Interventional cardiology	☐	Radiation oncology	☐
Interventional radiology	☐	Other, please specify:	☐
Indication/patient population (please provide as much detail as possible, including age range, sex, medical condition including severity/stage/grade, where applicable).			
Describe the new practice, e.g., utility or intended purpose of the radionuclide, diagnostic tool, radiotherapy technique, interventional radiology technique.			
Describe the **treatment(s)/practice(s)** which the new practice will **replace**, e.g., best medical care, another treatment or diagnostic practice.			
Briefly describe the **rationale** for the introduction of the new practice. Please provide supporting references.			

How established is the proposed practice?	New/Novel practice	☐
	New practice to Ireland, but well-established practice elsewhere	☐
	Existing technology/methodology in Ireland, but new indication	☐
	Existing technology/methodology in Ireland, but new population	☐
Does this practice involve a **significant change** (increase or decrease) in dose relative to current care?	Yes	☐
	No	☐
If yes, please provide details:		
Is this practice used in **other countries** for the proposed indication / patient population?	Yes	☐
	No	☐
If yes, please provide details on these countries, their practices (e.g. relevant clinical guidelines, SOPs etc.) and whether the practice has been generically justified (if known):		
For **radiation oncology practices only**: does the fractionation or target volume change?	Yes	☐
	No	☐
If yes, please provide details:		
Does the introduction of the new practice give rise to new concerns or alleviate existing concerns, regarding **public and/or occupational exposures**?	Yes	☐
	No	☐

If yes, please provide estimates of public and/or occupational exposure and outline any risk mitigating procedures/controls that are or shall be put in place:

Section 2. Additional supporting documentation

Additional documentation may be submitted to support an application for generic justification. Please indicate any additional documentation you intend to submit for consideration.

☐ Supporting studies, reviews or clinical/professional guidelines.
☐ Technical, regulatory or commercial information
(Please list website addresses here:)

Section 3. Declaration	
By submitting, I declare that the information I have provided in this form is true to the best of my knowledge and belief. The undertaking or affiliated organisation is aware that I am making this submission on its behalf.*	
Name (**print**)	
Job Title	
Contact number	
Signed (or e-signed)	
Date	

- **Email** form to: radiationjustification@hiqa.ie
- **Telephone**: 01 828 6700

* Please note: Names of undertakings or affiliated organisations will be included in the final HIQA publications on generic justification. Any concerns regarding this may be directed to the evidence review team at radiationjustification@hiqa.ie

Published by the Health Information and Quality Authority (HIQA).

For further information please contact:

Health Information and Quality Authority

George's Court

George's Lane

Smithfield

Dublin 7

D07 E98Y

+353 (0)1 8147400

info@hiqa.ie

www.hiqa.ie