Health Information and Quality Authority
An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Health Technology Assessment (HTA) Expert Advisory Group Meeting (NPHET COVID-19 Support)		
Meeting no. 15 : Monday 26th April 2021 at 11:00		
(Zoom/video conference)		
(DRAFT) MINUTES		
Attendance:		
Chair	Dr Máirín Ryan	Director of Health Technology Assessment (HTA) & Deputy Chief Executive Officer, HIQA
Members via video conference	Prof Karina Butler	Consultant Paediatrician and Infectious Diseases Specialist, Children's Health Ireland & Chair of the National Immunisation Advisory Committee
	Dr Jeff Connell	Assistant Director, UCD National Virus Reference Laboratory, University College Dublin
	Dr Eibhlín Connolly	Deputy Chief Medical Officer, Department of Health
	Prof Máire Connolly	Specialist Public Health Adviser, Department of Health and Professor of Global Health and Development, National University of Ireland, Galway
	Prof Martin Cormican	Consultant Microbiologist & National Clinical Lead, HSE Antimicrobial Resistance and Infection Control Team
	Ms Sinead Creagh	Laboratory Manager at Cork University Hospital & Academy of Clinical Science and Laboratory Medicine
	Dr John Cuddihy	Specialist in Public Health Medicine & Interim Director, HSE- Health Protection Surveillance Centre (HPSC)
	Dr Lorraine Doherty	National Clinical Director Health Protection, HSE- Health Protection Surveillance Centre (HPSC)
	Ms Josephine Galway	National Director of Nursing Infection Prevention Control and Antimicrobial Resistance AMRIC Division of Health Protection and Surveillance Centre
	Dr Cillian de Gascun	Consultant Virologist & Director of the National Virus Reference Laboratory, University College Dublin
	Dr James Gilroy	Medical Officer, Health Products Regulatory Authority
	Dr David Hanlon	General Practitioner & National Clinical Advisor and Group Lead, Primary Care/Clinical Strategy and Programmes, HSE
	Dr Patricia Harrington	Deputy Director, HTA Directorate, HIQA
	Dr Derval Igoe	Specialist in Public Health Medicine, HSE- Health Protection Surveillance Centre (HPSC)
	Prof Mary Keogan	Consultant Immunologist, Beaumont Hospital & Clinical Lead, National Clinical Programme for Pathology, HSE
	Mr Andrew Lynch	Business Manager, Office of the National Clinical Advisor and Group Lead - Mental Health, HSE
	Dr Gerry McCarthy	Consultant in Emergency Medicine, Cork University Hospital & National Clinical Lead, HSE Clinical Programme for Emergency Medicine
	Prof Paddy Mallon	Consultant in Infectious Diseases, St Vincent's University Hospital & HSE Clinical Programme for Infectious Diseases
	Prof Cara Martin*	Assistant Professor in Molecular Pathology and Tumour Biology at the Department of Histopathology, Trinity College Dublin. HSE ADT Validation Scientific Lead
	Dr Des Murphy	Consultant Respiratory Physician & Clinical Lead, National Clinical Programme for Respiratory Medicine, HSE

	Dr Sarah M. O'Brien	Specialist in Public Health Medicine, Office of National Clinical Advisor & Group Lead (NCAGL) for Chronic Disease
	Dr Gerard O'Connor	Consultant in Emergency Medicine, Mater Misericordiae University Hospital HSE Clinical Programme for Emergency Medicine
	Ms Michelle O'Neill	Deputy Director, HTA Directorate, HIQA
	Dr Margaret B. O'Sullivan	Specialist in Public Health Medicine, Department of Public Health, HSE South & Chair, National Zoonoses Committee
	Dr Dónal Sammin*	Director of Laboratories, Department of Agriculture, Food and the Marine
	Dr Lynda Sisson	Consultant in Occupational Medicine, Dean of Faculty of Occupational Medicine, RCPI & HSE National Clinical Lead for Workplace Health and Well Being
	Prof Susan Smith	Professor of Primary Care Medicine, Royal College of Surgeons in Ireland
	Dr Patrick Stapleton	Consultant Microbiologist, UL Hospitals Group, Limerick & Irish Society of Clinical Microbiologists
	Dr Conor Teljeur	Chief Scientist, HTA Directorate, HIQA
In attendance	Dr Laura Comber	HTA Research Analyst, HTA Directorate, HIQA
	Dr Christopher Fawsitt	Senior Health Economist, HTA Directorate, HIQA
Secretariat	Ms Debra Spillane	PA to Dr Máirín Ryan, HIQA
Apologies	Dr Ellen Crushell	Consultant Paediatrician, Dean, Faculty of Paediatrics, Royal College of Physicians of Ireland & Co-National Clinical Lead, HSE Paediatric/Neonatology Clinical Programme
	Dr Vida Hamilton	Consultant Anaesthetist & National Clinical Advisor and Group Lead, Acute Hospital Operations Division, HSE
	Dr Siobhán Kennelly	Consultant Geriatrician & National Clinical & Advisory Group Lead, Older Persons, HSE
	Ms Sarah Lennon	Executive Director, SAGE Advocacy
	Prof Simon More*	Professor of Veterinary Epidemiology and Risk Analysis, UCD
	Dr Deirdre Mulholland	Consultant in Public Health, National Clinical Lead for Knowledge, Evidence and Quality Improvement, Office of the National Clinical Director of Health Protection
	Dr John Murphy	Consultant Paediatrician & Co-National Clinical Lead, HSE Paediatric/Neonatology Clinical Programme
	Dr Michael Power	Consultant Intensivist, Beaumont Hospital & Clinical Lead, National Clinical Programme for Critical Care, HSE

**For the purposes of this meeting only*

Proposed Matters for Discussion:

1. **Welcome**

   The Chair welcomed all members. Apologies recorded as per above. Noted that three additional individuals joined the meeting for this topic, Professor Cara Martin, Assistant Professor of Molecular Pathology and Tumour Biology in Trinity Colleg, and scientific lead on HSE ADT validation studies, Dr. Donal Sammin, Director of Laboratories in the Department of Agriculture, Food and Marine. Professor Simon More from IEMAG was also part of the EAG for this provided input to the evidence summary.

2. **Conflicts of Interest**

One potential perceived conflict of interest was raised during the meeting from Prof Patrick Mallon: Prof Mallon's institution, University College Dublin, had received funding from Abbott Diagnostics for research into COVID19 diagnostic antibody testing. This research has been published in peer review, open access literature (published March 26th 2021; https://doi.org/10.1093/ofid/ofab122).

3. Minutes

The minutes of 22nd March 2021 and 30th March 2021 were approved as an accurate reflection of the discussions involved. The minutes of 6th April 2021 were also approved subject to a correction in the meeting number from 13 to 14.

4. Work Programme

The group was provided with an overview of the current status of the work programme including:

No.	Review Questions	Status of work	NPHET date
1	Serial RADT testing - meat processing plants	Drafted	29 April 2021*
2	Preventive interventions pre infection with SARS-CoV-2	Ongoing	6 May 2021
3	Modelling ROM for those travelling into Ireland	Ongoing	13 May 2021#
4	Update – Duration of protective immunity (protection from reinfection) following SARS-CoV-2 infection	To start 4 May	27 May 2021
5	Guidance on mass gatherings	To start 4 May	27 May 2021
6	Review of international public policy response for update	To start 8 June	17 June 2021
7	- Database	Ongoing - weekly	22 April 2021
	Public health guidance: - vulnerable groups - LTCFs	Ongoing	

* for submission to HSE RADT Working Group, # for submission to NCDHP

5. Presentation on serial RADT testing in meat processing plants (CT), including presentation by Prof Cara Martin on data from the meat processing plant validation study *(for discussion)*

The EAG were reminded that the HSE Antigen Test Working Group had previously requested that HIQA conduct an evidence synthesis and formulate advice with input from the EAG to address the following policy topic:

"What is the impact on transmission risk and resource requirements of different approaches to serial testing using rapid antigen detection tests (RADTs) in meat processing plants?"

Input received from the Irish Business and Employers Confederation (IBEC) was presented to the EAG.

The following points were raised for clarification following these presentations:

- It was clarified that the validation study undertaken involved the direct head to head comparison of RADT and RT-PCR, serial testing was not assessed. It was noted that repeated self-sampling may improve accuracy overall which will be informed by the roll out of RADT in meat processing plants currently underway.
- The WHO outlines a desired sample size of 100 positive and 300 negative tests for validation studies. Due to logistical constraints the validation study was ceased once stability of sensitivity rates was reached.
- The processing of the validation tests across a number of sites may be a limitation.
- In terms of the transformation of viral loads, it was noted that the assays are intended for qualitative analysis rather than quantitative.
- The confidence intervals presented within the report were noted to be wide. It was clarified that these confidence intervals represent results from simulation modelling rather than statistical tests and hence have a different interpretation, with their primary aim to highlight uncertainty in the modelled estimates which arises due to uncertainty in the parameter estimates. It was agreed to clarify this in the report.
- It was clarified that the model treated all individuals as susceptible at the start of the simulation, with individuals previously infected within the model not susceptible to becoming infected.
- The background incidence may be more easily interpreted in the format of incidence per 100,000 given this is how it is regularly presented by NPHET. It was agreed to clarify this in the report.
- The delay in RT-PCR confirmation within the model was assumed to be on average two days, with some individuals getting results prior to this and some after.
- The proportion who are infectious is uncertain given a lack of a standard test to inform this parameter. It was agreed to add a sensitivity analysis of this parameter estimate.
- While the model takes account of an average facility, as is necessary for such an analysis, meat processing plants are heterogeneous in terms of products, processes and operational environments which will impact on risk. Acceptability for stakeholders is also unlikely to be homogenous or randomly distributed across plants.

6. Advice: Serial RADT testing in meat processing plants (PH) *(for discussion)*

The following points were raised for discussion following this presentation:

- RADT-based testing should be seen as an addition to the suite of risk mitigation measures rather than a replacement.

- Air circulation and occupancy levels in certain areas of certain plants present an elevated risk for SARS-CoV-2 transmission. Meat processing plants are not uniform, with differences in activities and products contributing to differences in operational environments and occupancy levels. In addition, individual meat plants are compartmentalised for reasons of animal welfare and food hygiene. In Ireland and internationally there is significant evidence of within-plant clustering, with large clusters of cases occurring in meat cutting rooms. It was highlighted that there are long-standing EU legislative requirements for the industry to maintain an ambient temperature of ≤12˚C in the meat-cutting rooms. The industry operational norm has therefore been to recirculate chilled air, minimising the number of air changes per hour to achieve this temperature requirement. Recognising that recirculation of air may contribute to super-spreading events by facilitating airborne spread of SARS-CoV-2, the industry has acted to mitigate transmission risk by increasing the number of air changes per hour. However, this will not be possible with the existing air-conditioning infrastructure in the warmer summer months.

- Re-evaluation of environmental requirements, for example ambient air temperatures, would require approval by international regulatory bodies and trading partners. Significant capital investment is required to facilitate upgrading of air handling units and retrofitting of meat processing plants. However, these changes will not be in place until summer 2022 as multisite validations will be required to demonstrate their efficacy in reducing the risk of transmission of human respiratory viruses without compromising food safety. Therefore additional measures are required to reduce this imminent risk of increased transmission during the warmer summer months.

- Acceptability of RADT-based serial testing to all relevant stakeholders is a crucial consideration. Given the differences within and between meat processing plants, such acceptability is unlikely to be consistent across the sector. In particular, concerns were raised about income protection and security for certain meat processing plant employees. It was noted that issues have previously been highlighted in relation to sick pay within the sector by the Migrants Rights Centre Ireland and trade union representatives for meat processing plant employees. Uncertainty over income may create disincentives for engagement with voluntary serial testing, given the requirement to stay away from work in the context of self-isolation for the individual case, and restriction of movements for close contacts.

- The positive predictive value of RADT testing is impacted by the incidence of COVID-19; with a higher rate of false positives when incidence is low. This highlights the requirement for RT-PCR confirmation of positive antigen tests in the context of serial testing. If there are high numbers of false positives, there may be challenges to the ongoing acceptability of RADT-based testing given requirements for self-isolation and restriction of movement, while awaiting reconciliation with confirmatory RT-PCR tests. This will be increasingly true with lower community incidence and increasing vaccination coverage.

- Serial testing is only one of a suite of measures that can be used to reduce the risk of transmission in a facility. That suite of measures must take into account the need to facilitate the adherence of infected individuals in to requirements for self-isolation as a means to reduce the introduction of SARS-CoV-2 into the workplace. When infectious individuals present in the workplace, testing is not a solution to overcome the inherent risk of transmission.

- The current strategy of monthly RT-PCR based serial testing appears to be relatively inefficient compared with more frequent RADT-based testing. RT-PCR testing is associated with longer test turnaround time and more invasive sample collection. While the use of RADT-based serial testing may offer a means to overcome these shortcomings, an effective testing programme be dependent on acceptability, uptake and adherence to testing schedules.

- The uptake of RADT-based testing by workers during the HSE-based validation studies was noted to be very high, with good acceptability of mid-turbinate nasal swabs compared with combined oropharyngeal nasopharyngeal swabs currently used in RT-PCR-based testing. However, it was noted that there have been challenges with the roll-out of RADT-based serial testing which has been offered to the meat-processing plants currently engaged in the HSE PCR-based serial testing programme. All aspects of RT-PCR-based testing are managed by the HSE Test and Trace programme with sampling undertaken by the National Ambulance Service. In contrast, in the roll-out of RADT-based testing, there is a requirement for the meat processing plants to manage the sampling, testing and reporting processes themselves as well as maintaining quality standards in testing. This has posed logistical and operational challenges at the level of the plant, compounding other commercial challenges the sector is experiencing due to both Brexit and COVID-19. Furthermore, there are concerns that complacency or fatigue may be a factor secondary to the relatively low level of case detection in recent testing rounds. The communication of nuances relating to test accuracy, duration of infectiousness, and frequency of testing is challenging. It was noted that the Department of Agriculture, Food and the Marine has had ongoing engagement with meat processing plants in an effort to improve uptake and communicate the importance of testing frequency.

- In light of the issues encountered in the roll-out of serial RADT-based testing in meat processing plants, a transitional implementation should be considered alongside the current strategy of monthly RT-PCR testing. Maintaining monthly RT-PCR would ensure continued case detection while any issues with the adoption of RADT-based testing are identified and addressed. This approach would also allow evaluation of RADT-based serial testing in real world environments before considering a change in the overall serial testing strategy.

- A risk-based approach may have merit whereby frequency of testing is dictated by plant level factors including the presence of work areas in which there is a combination of high occupancy and relatively poorer ventilation, such as in boning halls, and or

disease factors such as community incidence. Furthermore, a standard outbreak management approach could be considered whereby a certain number of positive RADTs within a plant triggers the use of RT-PCR sweep testing.

- If RADTs are to be used as part of the serial testing programme, there is a need for a national plan in relation to quality control, RADT batch acceptance and batch verification. These processes are not currently standardised; standardisation would be important should such testing regimens be implemented. Furthermore, standardisation of training and competency-based assessment for the conduct of such testing would be required; in particular given that the accuracy of RADT-based testing is highly dependent on test processing times.

- Informed consent and confidentiality with the implementation of serial testing regimens were highlighted as important issues. The Department of Agriculture, Food and the Marine has developed and agreed guidelines with the HSE and the industry. It was emphasised that all testing is voluntary and is on the basis of informed consent. To facilitate same, consent forms have been written in plain language and translated into 12 of the most common languages identified in the plants. Processes to maintain employee confidentiality have also been implemented. It was acknowledged that it was essential that these ethical obligations continue to be protected for workers.

- Given the extent of the measures required to mitigate transmission risk in meat processing plants and the potential for outbreaks in these settings to seed outbreaks in the community, it was suggested that reconsideration could be given to prioritising vaccination of meat plant workers.

- It should be emphasised that the findings of this evidence synthesis are specific to meat processing plants which constitute a higher risk environment. The results should not be considered generalisable to other settings or populations. The model parameters used are specific to this population and therefore cannot be used to directly inform other potential testing regimens outside of this setting. Context-specific issues would need to be considered and evaluated if adopting RADT-based testing in other settings.

7. Presentation on protocol Modelling ROM for those travelling into Ireland (CT) *(for discussion)*

The EAG was informed that NPHET had requested that HIQA work with National Clinical Director of Health Protection to address the following policy topic:

"To examine whether a single test at Day 5 post arrival in Ireland remains the most appropriate approach to testing for those travelling from non-designated States, who are subject to home quarantine"

This policy question was used to formulate the following specific research questions:

1. What is the risk of SARS-CoV-2 infection in people travelling into Ireland (by sea and air) from designated and non-designated states?

2. Is the risk of SARS-CoV-2 infection proportional to the incidence of COVID-19 in the origin country?

3. How do different choices for duration of restriction of movement and timing of testing of people travelling into Ireland impact on number of infectious person-days in the community?

The following points were raised as matters for clarification or discussion by the EAG:

- The parameter on timing of pre-arrival testing was queried. The current practice of testing within 72hrs prior to arrival into Ireland, could potentially be too long when other countries are requiring a test within 48hrs prior to arrival. It was clarified that as we do not know when exposure occurs, a conservative approach is to assume that any exposures happened in the course of transit and that day zero is the day of arrival in Ireland.
- The EAG discussed that the impact of antibody testing for protective immunity may help to identify individuals with a low probability of developing SARS-COV-2. This would provide predictive information, however it is not known what level of antibodies is required to provide immunity, particularly for protection against new variants of concern. Other components of the immune system are also important. It was highlighted this is not within the scope of the analysis but it could be considered as a discussion point.

8. Meeting Close

The Chair thanked the EAG members for their contributions and highlighted the meeting on 4th May would be on a Tuesday with an earlier start time of 9.30am due to the Public Holiday The EAG would be addressing the evidence summary around preventive interventions and modifiable risk factors prior to infection with SARS-COV-2.

a) AOB
b) Date of next meeting: Tuesday 4 May 2021 at earlier time of 09.30am

Meeting closed at 13.02