NATIONAL OFFICE FOR RESEARCH ETHICS COMMITTEES

National Research Ethics Committee

NREC-MD Meeting Minutes

15 July 2024

Attendance

Name	Role
Prof. Barry O'Sullivan (Chair)	Chair, NREC-MD
Prof. Declan Patton (Deputy Chair)	Deputy Chair, NREC-MD
Dr Caitriona Cahir	Member, NREC-MD
Dr Ruth Davis	Member, NREC-MD
Dr Owen Doody	Member, NREC-MD
Dr James Gilroy	Member, NREC-MD
Dr Gloria Kirwin	Member, NREC-MD
Ms Orla Lane	Member, NREC-MD
Prof. Cara Martin	Member, NREC-MD
Mr Billy McCann	Member, NREC-MD
Dr Sarah McLoughlin	Member, NREC-MD
Dr Declan O'Callaghan	Member, NREC-MD
Dr Clare O'Connor	Member, NREC-MD
Dr Paul O'Connor	Member, NREC-MD
Dr Joanne O'Dwyer	Member, NREC-MD
Prof. Mahendra Varma	Member, NREC-MD

Ms Simone Walshe	Member, NREC-MD
Mr Peter Wolfe	Member, NREC-MD
Dr Lucia Prihodova	Programme Manager, National Office for Research Ethics Committees
Dr Louise Houston *	Project Officer, National Office for Research Ethics Committees

*Drafted minutes.

Apologies: Prof. Mary Sharp, Dr Daniel Coakley, Dr Mirielle Crampe, Dr Frank Houghton, Prof. Tom Melvin, Prof. Therese Murphy, Mr Damian Owens

Quorum for decisions: Yes

Agenda

1. Welcome (Chairperson) and apologies:
2. Report on Committee business
3. Minutes of previous meeting
4. Declarations of interest
5. 24-NREC-MD-016
6. 24-NREC-MD-017
7. 24-NREC-MD-018
8. 24-NREC-MD-019
9. 24-NREC-MD-020
10. 23-NREC-MD-010-SM3
11. AOB

- Prof. Barry O'Sullivan welcomed the Committee and acknowledged apologies sent and opened the meeting.
- NREC Committee Business Report: The Committee noted the report.
- Minutes of the previous meeting (20 June 2024) were approved.
- Matters arising from the previous meeting: none
- Declarations of interest:
  - Dr Clare O'Connor (24-NREC-MD-017) did not read the documentation associated with the application and vacated the meeting while the study was under discussion.

Applications

24-NREC-MD-016

- Principal Investigator: Prof Ray McDermott
- Study title: An interventional, prospective clinical study protocol for testing RNA extracted from FFPE tumor tissue specimens taken from patients with Intermediate risk Non-Muscle-Invasive Bladder Cancer (IR-NMIBC) for FGFR alterations, using the QIAGEN therascreen® FGFR RGQ RT- PCR Kit, to determine molecular eligibility (FGFR gene alterations detected) for enrolment onto Janssen's Phase 3 clinical trial of the FGFR inhibitor, erdafitinib (MoonRISe-1 number 42756493BLC3004).
- Lead institution: St. Vincent's University Hospital, Dublin
- Sponsor: Qiagen Manchester Ltd.
- NREC-MD Decision
  - *Request for Further Information*
- Further Information Requested:

- While the NREC-MD appreciate that the eligibility for enrolment will be determined by multiple molecular tests, information about participation in the performance study is not clearly presented and is lacking in candour. The Committee further noted that "Privacy appendix to molecular eligibility testing informed consent" has been added to the consent form and while it clarifies the areas of future research, it addresses the current study in only limited detail. To that end, the NREC-MD requests that participants are:
  - Explicitly informed that they are asked to participate in a performance study undertaken by Qiagen and that the sponsor may derive commercial benefits from the study
  - Explicitly informed about any risks associated with the study, eg false positives or negatives
  - Explicitly asked to consent for participation in the performance study
  - Explicitly asked to indicate their preference in relation to future use of data and samples (please refer to Guidance on use of biological samples and associated data for more information)

24-NREC-MD-017

- Principal Investigator: Dr Noel Gerard McElvaney
- Study title: AAV8 TAb Assay for Eligibility in the ITL-3001-CL-101 Clinical Trial
- Lead institution: Beaumont Hospital
- Sponsor: ARUP Laboratories
- NREC-MD Decision

- *Request for further information*

- Further Information Requested:
- The NREC-MD requests a clarification on the recruitment and consenting process. Please provide details on who will be approaching potential participants, their qualifications, and on any procedures which will be in place to minimise any bias posed by the recruitment process.
- The NREC-MD requests more information / clarity on cut-off values, ie what happens to those falling in between the cut-off ranges, and possible false positives/ false negative rates with the assay and the potential impact of same with respect to enrolment.
- Page 17 of the Performance Study Plan states that “80 subjects will be tested with the AAV8 TAb assay”. However, elsewhere in the documentation e.g. Clinical Trial Protocol, states that only 30 participants will be tested. Please clarify this discrepancy. If applicable, confirm if 30 samples are adequate to establish performance characteristics of the assay.
- Please clarify the cut-off values for the assay used in the study.
- The NREC-MD Application Form Section F21 suggests the GP will not be informed of the patient’s participation in the study, however the PIL/ ICF contradicts this and suggests the GP will be informed. Provide a clarification and a copy of a GP letter if applicable.
- The NREC-MD Application Form Section J1 suggests that participants of child-bearing potential or pregnant or breastfeeding participants will not be included in this study. However, the PIL/ICF includes detailed information in relation to pregnancy and pregnant individuals. Please update Section J1 of the Application Form accordingly.
- Please confirm how long ARUP will retain personal data and biological samples and for what purposes.
- Please confirm that the Clinical Trials of Investigational Medicinal Product (CTIMP) component of this study will be submitted to NREC-CT for review.
- The PIL/ICF to be updated to include information on the performance study and the investigation device used within this study. As discussed with the sponsor during pre-submission engagement, this could be addressed by the use of a separate PIL/ICF for the performance study.
- The PIL/ICF to be updated to state that the AAV8 DetectCDx assay is investigational assay and not yet approved for clinical use.
- The PIL/ICF to be updated to include information on the risks of false positives/ negatives to clearly state
    - the likelihood of false positives/ negatives,
    - that there are potential side effects from investigational drug if a participant is exposed to the IMP/ from being involved in the control arm as a result of a false positive result,
    - the risks associated with false negative being excluded from a study which they could potentially benefit from.
- The PIL/ICF states that “optional reserve blood samples” may be collected and used for future research. However, p8 of the PIL/ICF states that these optional samples are “are

required for your safety and/or for future research". Please clarify what samples are optional and which necessary for safety and update relevant documentation accordingly.

- The PIL/ICF states that "an additional consent form" will need to be signed for optional reserve blood samples. Provide this for Committee review.
- The NREC-MD requests a financial disclosure form is provided for both investigators.
- The NREC-MD requests a copy of draft site agreement is provided.

24-NREC-MD-018

- Principal Investigator: Dr Austin Duffy
- Study title: Clinical performance study for use of the FOLR1 (2.1) Clinical Trial Assay in Study IMGN853-0424: A Randomized Phase 2 Study of Ocular Toxicity Evaluation and Mitigation During Treatment with Mirvetuximab Soravtansine in Patients with Recurrent Ovarian Cancer with High Folate Receptor-Alpha Expression
- Lead institution: Mater Misericordiae University Hospital
- Sponsor: Immunogen Inc.
- NREC-MD Decision
  - *Request for further information*
- NREC-MD Comments:
- Section E of the Application Form to be updated to include details relating directly to the Performance Study only.
- Participant's hospital consultant / GP to be informed of their patient's participation in the performance study. Participant's consent to share the information on their participation with their hospital consultant / GP should be sought and a copy of the letter sent to the hospital consultant / GP should be provided to the National Office.
- Section M1 of the Application Form states that genetic data will be obtained. However, given that this assay will be used to detect protein rather than DNA or RNA, it is unclear from the information provided what genetic data will be obtained. Please clarify.
- Page 1 of the PIL/ICF: The line "This drug has been shown to have benefit in patients who, like you, have ovarian cancer" to be removed as the drug may not have shown benefits in certain types of ovarian cancer.
- The PIL/ICF to be updated to include information on the risks of false positives/ negatives to clearly state
  - the likelihood of false positives/ negatives
  - that there are potential side effects from investigational drug if a participant is exposed to the IMP/ from being involved in the control arm as a result of a false positive result
  - the risks associated with false negative being excluded from a study which they could potentially benefit from.

- Please note NREC-MD will never request access to participant data. Please revise the PIL/ICF accordingly.
- The NREC-MD noted that individuals will be recruited and consented by the Principal Investigator (PI). The Committee suggests that for participants in current care of the PI this activity be assigned to an authorised designee of the Principal Investigator (as per ISO 14155:2020), who is a member of the investigating team appropriately qualified under national law (as per Article 59(2)(c) of the In Vitro Medical Device Regulation (EU) 2017/746) to minimise any perception of coercion.
- It is currently unclear how many participants will be recruited for this study. Section F of the Application Form indicates that 10 participants will be recruited from Ireland, 100 overall. However, a larger a figure of 310 participants is cited in Document 31. Please confirm the number of participants to be recruited in the performance study over and in Ireland only. Section F2-F5 of the Application Form should be updated accordingly.
- Site suitability forms to be updated to include information on the suitability of the site to recruit and consent participants, handle and store samples and data and perform biopsies.
- Revise the PIL and ICF to ensure they are in compliance with data protection regulations and legislation, including the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), that i) consent for future use of data be 'unbundled' (i.e. separate and optional) from the other consent items, ii) consent can only be obtained where future research is defined, such that participants are fully informed, and/or iii) when the future research is currently undefined, that an option is provided to enable participants to consent to be contacted with regard to future research. The NREC-MD advises the applicant that subsequent research ethics review must be sought for specific research once clearly defined.
- The references to future use of stored samples throughout the Application Form and the PIL/ICF are inconsistent and unclear. Please confirm is samples will be retained and used for future research. If so, the Application Form and PIL/ICF must be updated accordingly.
- Section 3 of the Statement of Compliance for Data Protection (Document 24) provided, indicates that participants data will be de-identified. However, other documentation indicates that the data will be pseudonymised. Clarify this discrepancy and update the documentation accordingly.
- All reasonable participant expenses such as parking etc for those undergoing additional biopsy to be reimbursed. All compensation should be outlined in the PIL.
- Section Q1 of the Application Form to be updated to include information on the insurance in place for compensation in the event of a claim made by or on behalf of a participant in the case of an event or injury.
- Section R1 of the Application Form to be updated to confirm funding has been secured for the performance study itself.

24-NREC-MD-019

- Principal Investigator: Dr Rajendra Ramsamooj
- Study title: Oncomine™ Dx Express Test Clinical Performance Study Protocol (NTRK), Solid Tumor (FFPE), Danube, Project Number PRJ0003987
- Lead institution: Life Technologies Clinical Service Lab Inc.
- Sponsor: Life Technologies Corporation, part of Thermo Fisher Scientific
- NREC-MD Decision
  - *Request for Further Information*
- Further Information Requested:
- Section E of the Application Form states that samples will be randomised. However, it is unclear how samples will be randomised in the context of this study where there is no intervention. Confirm.
- The NREC-MD notes that samples will be de-identified. Confirm what this means, anonymised, pseudonymised etc.
- The NREC-MD notes that one of the aims of the study is to establish the clinical validity of the ODxE Test based on clinical response of ODxE Test identified NTRK gene fusion-positive patients. Given that samples will be de-identified, clarify how this will be possible.
- Section J1 of the Application Form is currently incomplete. Complete this section for breastfeeding individuals.
- Sections K6, K7 and K9 of the Application Form state that personal data is not collected as part of this study. As tissue samples and blood are considered personal data, these sections must be completed.
- Section K14 of the Application Form should be updated to select ‘other’ and tissue samples should be noted.
- Section L16 of the Application Form to be completed.
- While the Committee noted that the PI is committed to the highest standard in research integrity, given the Principal Investigator as an employee of the sponsor, please outline what is the conflict of interest management plan for this study. Please update section R2 and R3 of the Application Form accordingly and provide a completed declaration of interest for the PI.
- The NREC-MD noted that the insurance relates to the initial clinical trial and the period is up to 31 December 2019. It is unclear if this policy covers the study period up to 31 December 2025 and additionally the future use of samples. Clarify and confirm if this performance study requires any specific insurance policy, if no, provide justification.
- Confirm that only samples from patients who have indicated ‘Yes’ for future storage and use (Page 23 of Participant Information Leaflet/Informed Consent Form (PIL/ICF)) will be used. How will the sponsor have oversight of this?

- Given that the initial consent for future use was obtained before IVDR implementation and is broad in its wording, please comment on how the existing consent aligns with the requirements set out in the Health Research Regulations 2018. Please consult the National Office Guidance on use of biological samples and data. Please also comment whether there is scope to seek specific consent for this performance study from participants whose samples are to be included in this new study.
- Page 19 of the PIL/ICF states that there is no expiration date to collect, use and share medical information. Confirm that all data collected and intended for use in the study was collected within the original study period.
- Please clarify the process for withdrawal of consent. If the data is to be de-identified does this mean participants can no longer be linked to their samples and therefore, no longer withdraw their data. The existing PIL/ICF did not seek specific consent for de-identification. Therefore, please comment if the proposed analysis is outside of the consent provided by participants.

24-NREC-MD-020

- Principal Investigator: Prof Ronan Cahill
- Study title: CLASSICA: Validating AI in Classifying Cancer in Real-Time Surgery - Study 2
- Lead institution: Mater Misericordiae University Hospital
- Sponsor: University College Dublin
- NREC-MD decision:
  - *Request for further information*
- Further Information Requested:
- It is currently unclear how many participants will be recruited for this study. Section F of the Application Form indicates that 127 participants will be recruited from Ireland. However, the Site Suitability Forms state that only 45 participants will be recruited from Ireland. Moreover, the PIL/ICF states that 125 and 100 participants will be recruited. Clarify this discrepancy and update all documentation accordingly.
- In the PIL/ICF, the Section *"Why is this study being done?"* is overly technical and should be revised and simplified to ensure readability and accessibility.
- The PIL/ICF states that "1 in 5 tumours that contain cancer will not be detected on biopsy". This statistic may be worrying and stressful to potential participants. Please confirm if it is standard practice to inform participants of this statistic. If not, this should be reworded to lessen anxiety and undermine trust in current practice in prospective participants.
- In the PIL/ICF, information on 600 participants recruited to a second study to be removed as may be confusing for participants.

- In the PIL/ICF, an email address to be provided for the Principal Investigator (PI) and Research Nurse, rather than just a phone number and address.
- While the Committee noted that the PI is committed to the highest standard in research integrity, given the multiple roles held by Prof. Cahill in the project, including funding for the study and the declared conflict, please outline what is the conflict of interest management plan for this study.
- The CVs provided for Prof John Burke and Prof Peter Neary have very little detail on previous clinical trial experience. Provide further detail to ensure suitability.
- The CV provided for Prof John Burke does not contain a reference to GCP training. Confirm this training has been / will be completed.
- Confirm if data will be pseudonymised or anonymised. Both terms are used interchangeably throughout the application. If anonymised, the PIL/ICF should be updated to obtain explicit consent for this.

23-NREC-MD-010-SM3

- Principal Investigator: Dr Darren Mylotte
- Study title: Evolut™ EXPAND TAVR II Pivotal Trial
- Lead institution: University Hospital Galway
- Sponsor: Medtronic Bakken Research
- NREC-MD Decision
  - *Favourable*

AOB

- The Chairperson thanked the Committee and closed the meeting.