NATIONAL OFFICE FOR RESEARCH ETHICS COMMITTEES

National Research Ethics Committee

NREC-MD Meeting Minutes

16 May 2024

Attendance

Name	Role
Prof. Mary Sharp (Deputy Chair)[X]	Deputy Chair, NREC-MD
Prof. Declan Patton (Deputy Chair)[X]	Deputy Chair, NREC-MD
Dr Mireille Crampe	Member, NREC-MD
Dr Ruth Davis	Member, NREC-MD
Dr Frank Houghton	Member, NREC-MD
Ms Orla Lane	Member, NREC-MD
Prof. Cara Martin	Member, NREC-MD
Mr Billy McCann (PPI)	Member, NREC-MD
Dr Sarah McLoughlin (PPI)	Member, NREC-MD
Dr Declan O'Callaghan	Member, NREC-MD
Prof. Susan O'Connell	Member, NREC-MD
Dr Clare O'Connor	Member, NREC-MD
Dr Paul O'Connor	Member, NREC-MD
Prof. Jim O'Neill	Member, NREC-MD
Mr Damien Owens	Member, NREC-MD

Mr Peter Woulfe	Member, NREC-MD
Dr Lucia Prihodova *	Programme Manager, National Office for Research Ethics Committees

X Prof. Mary Sharp chaired the NREC meeting from 10-11am (agenda item 1-8) and Prof. Declan Patton from 11am-12.30pm (agenda items 9-13).

*Drafted minutes.

Apologies: Dr Caitriona Cahir, Dr Daniel Coakley, Dr Owen Doody, Dr James Gilroy, Dr Gloria Kirwan, Prof. Tom Melvin, Prof. Therese Murphy, Prof. Anne Parle McDermott, Ms Riona Tumelty, Prof. Mahendra Varma

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-015
6. 22-NREC-MD-038-SM2
7. 23-NREC-MD-028-R1
8. 22-NREC-MD-039-SM2-R1
9. 24-NREC-MD-008-R1
10. 24-NREC-MD-012-R1
11. 24-NREC-MD-013-R1
12. 24-NREC-MD-002-SM1
13. 23-NREC-MD-016-SM1
14. AOB

- Prof. Mary Sharp 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(s) (18 April 2024) were approved.
- Matters arising from the previous meeting: none
- Declarations of interest:

- Prof. Jim O'Neill (24-NREC-MD-008-R1) did not read the documentation associated with the applications and vacated the meeting while the study was under discussion.
- Prof. Jim O'Neill (23-NREC-MD-016-SM1) did not read the documentation associated with the applications and vacated the meeting while the study was under discussion.

Applications

24-NREC-MD-015

- Principal Investigator: Prof. Fergal Malone
- Study title: Use of the Fetal Antigen Non-Invasive Prenatal Testing (NIPT) Clinical Trial Assay to determine fetal red blood cell antigen status in the Janssen-sponsored Phase 3 IMP clinical trial.
- Lead institution: Rotunda hospital, Dublin
- Sponsor: BillionToOne, Inc.
- NREC-MD Decision
  - *Request for further information*
- Further information requested:
- The NREC-MD noted that the proposed device classification listed in the NREC-MD Application form section D5 is Class C and queried whether this classification has been approved by the HPRA.
- he NREC-MD Application form section F21 suggests the GP will not be informed of the patients participation in the study, however pg 26 the maternal PIL/ ICF contradicts this and suggests the GP will be informed. Provide a clarification and a copy of such GP letter if applicable.
- The NREC-MD noted that page 24 of the maternal PIL/ICF suggests use of social media and use of “an independent locator agency” to find out about the patients’ health status if they stop attending the clinic. The Committee requests clarification and justification for such approach.
- The NREC-MD noted that section J2 & J3 of the application form lists a small number of risks associated with the performance study as listed in the NREC application form. However the main risk could be significant e.g. incorrect results (false-positive) which could result in the mother and baby receiving treatment with IMP when there is no benefit to them. The Committee requests that the application form is updated accordingly.
- The NREC-MD noted that the PI or his delegate (NREC-MD Application form section G4) will obtain the informed consent. In line with best practice, participant recruitment should be performed by a suitably qualified member of the study team who is not involved in direct clinical care for the prospective participant.
- Furthermore, the NREC-MD requests that the information on the qualifications of the delegate is provided.

- The NREC-MD requests that participants are given minimum 24 hours to review and consider the Participant information Leaflet before their consent is sought.
- The NREC-MD noted that the application pack included additional brochures and leaflets to be used for recruitment that some of the recruitment brochures referred to FDA and request clarification on whether these will be used in Ireland.
- Furthermore, the NREC-MD requests that procedures for handling responses to advertisements are provided.
- The NREC-MD noted that NREC-MD Application form section G8 states that "ICF is available and can be provided in different languages and an interpreter will be available as needed." The Committee noted that participants without proficient English should be provided with a copy of a translated Participant Information Leaflet and Informed Consent Form and the translations must be completed by a certified translation provider. A copy of the translation certificates should be provided to the National Office.
- The NREC-MD noted that across the documentation, (eg NREC-MD Application form section G9; page 20 of maternal PIL/ICF), several references are made to retention of biological material of the pregnant participant (blood samples) for further research eg "research for possible diagnostic assay development". Furthermore the PIL/ICF states that anonymous data and samples can be used for purposes of scientific research. Please note that the Data Protection Act 2018 allows for the use of broad, not blanket consent when it comes to further processing of personal data for the purposes of health research. Consent for future use of data must be limited to a particular disease area or more generally in that area or a related area of health research and must be clearly described in the Participant Information Leaflet. An example would be limiting future use of study data to the disease and / or medicinal product / device being studied.
- If intended for unspecified future use, consent to anonymise all data related to the biological samples should be sought from participants. However, as it is questionable whether genetic information can be truly anonymised, future uses of blood samples need explicit consent and blanket consent (for unspecified research) is not valid.
- Please note that any future studies would be a subject to separate REC review.
- The NREC-MD noted that page 16 of maternal PIL/ICF states that "if you become pregnant during the study after your initial pregnancy, you must tell clinical staff immediately……by signing this consent, you agree to share relevant medical information about your pregnancy. You are free to change your mind at any time." As future pregnancy would fall outside the scope of the study, the NREC-MD requests that participant consent is sought with respect to any information taken related to future pregnancy.
- The NREC-MD noted that genetic information will be taken for the study related to the unborn child's blood type from the maternal blood sample (page 21 of maternal PIL/ICF) and requests clarification whether any future research is intended to be carried out on the genetic information of the child.
- The NREC-MD noted that the samples (two) will be stored for 15 years or unless potential participant asks for them to be destroyed, but this is not provided as an option in the consent section and requests the form is updated to facilitate this.

- Given the proposed length of storage of samples, the NREC-MD requests clarification on what will happen to the samples should BTO be acquired in the future.
- The NREC-MD noted that page 21 of maternal PIL/ICF states “in the unlikely event that your genetic information is released to other companies, applicable country laws may not fully protect you or your family from judgements based on genetic information,” and request clarification on how this risk is being mitigated.
- The NREC-MD noted that there will be transfer of personal data (and samples) outside of EU (to USA) to BillionToOne and Janssen and while data transfer is dealt with in the NREC application, it is not addressed in the maternal PIL/ICF. Notably, BillionToOne is not mentioned in the PIL despite the fact that it will receive pseudonymous personal data.
- The NREC-MD noted that information on participant rights concerning personal data is very vague (page 26 of maternal PIL, Privacy Appendix). While some data subject rights may be limited, the Committee requests that the limits are more clearly specified.
- Further to previous points, the NREC-MD requests that consent for future use of coded personal data is unbundled in the consent form.
- Similarly, the Committee requests that consent form includes consent for anonymisation of personal data if required for unspecified future use.
- The NREC-MD noted that it is not clear if the CTA study involves the use of the Clario eCOA App or if this only relates to participants of the Azalea study. However, the PIL/ICF states that Clario “may also use this information for its internal purposes such as quality assessment / improvement and customer service.” The Committee requests that this is optional and not a condition of participation in the study.
- The NREC-MD noted that the authorisation to use the data on the Clario App has no expiration date and can only be revoked by submitting a written request to the study staff. While it is understood that consent to processing data will take place until it’s withdrawn, it should not be indefinite and that there should be a defined data storage time limit. At the end of the storage time, data should be destroyed or irrevocably anonymised (and consent for this must also be obtained).
- The NREC-MD noted that the parent/guardian PIL/ICF submitted with the application pack relates to main clinical trial of investigative medicinal product (CTIMP) and did not feel appropriate to comment on it. All comments on PIL/ICF in this decision letter therefore relate to the Maternal PIL/ICF.
- The NREC-MD noted that the language used in the PIL/ICF is overly technical and uses some terms that are not explained (in particular ePRO is not explained anywhere). It also has references to NHS and the UK’s Information Commissioner’s Office in the Privacy Appendix that should be removed and replaced with relevant Irish references. The Committee requests that the document is revised for accessibility and accuracy.
- The PIL/ICF does not clearly address the Clinical Trial Assay (CTA) Performance Study, specify that the CTA is being studied or clearly explains that the CTA is one of the criteria being used to assess the individuals suitability to join the overall study.
- There are currently no individual consent lines for the performance study.

- To that end, the NREC-MD requests that a separate PIL/ICF is developed for the screening process, including the Clinical Trial Assay Performance Study and the associated CTIMP as participants may not be eligible or willing to proceed after undergoing the screening procedures. Alternatively, the current maternal PIL is to be amended to clearly identify the CTA as a preliminary procedure and to highlight the information specific to the CTA and the relevant consents related to same.
- Furthermore, if applicable, the maternal PIL/ICF should specify that child DNA analysis will be undertaken from the maternal blood.
- The NREC-MD noted that BillionToOne is not referred to at any stage in the maternal PIL and requests their role is clearly specified in the PIL/ICF.
- The NREC-MD noted that the following consent items could be considered to ensure explicit and unbundled consent is sought, eg: consent for blood test screening; consent for data/samples to be sent to the US; consent for possible use of samples to be used for future research, etc.
- The NREC-MD noted that the PIL/ICF states that “samples can be destroyed on request (unless they cannot be linked to you)”. The Committee requests clarification on how this could be possible given that the site maintains the link to identify participants.
- The NREC-MD noted that according to the PIL/ICF the Clario eCOA App – “If you withdraw your consent for study intervention only, you will still be expected to perform trial assessments, including ePRO completion. If you withdraw consent from the entire study, no further ePRO data completion is expected.” (page 23). The Committee requests clarification on what this statement means and that the statement is revised for accessibility.
- The NREC-MD noted that the Privacy Appendix states that the Sponsor for the study is based in Europe, but the address for Janssen is in the USA and it is clear that considerable amounts of personal data will be processed outside of EU.
- The NREC-MD noted that the certificate of insurance for BillionToOne has expired and requests an updated certificate is provided when renewed.
- The NREC-MD noted that the Clinical Trial Agreement and the budget are in draft form and request executed versions of these are provided when finalised.

23-NREC-MD-038-SM2

- Principal Investigator: Dr Matthew Barrett
- Study title: Comparison of Departmental Echocardiogram vs. Caption AI-driven Acquisition (CODEC-AI).
- Lead institution: St. Vincent's University Hospital, Dublin
- Sponsor: HSE
- NREC-MD Decision
  - *Favourable*

23-NREC-MD-028

- Principal Investigator: Prof. Joseph Butler
- Study title: Clinical and Radiologic Outcomes Associated with the use of SYMPHONY OCT System for the Treatment of Acute and Chronic Instabilities of the Craniocervical Junction, the Cervical Spine and the Upper Thoracic Spine.
- Lead institution: Mater Misericordiae University Hospital, Dublin
- Sponsor: University College Dublin
- NREC-MD Decision
  - *Favourable with conditions*
- Associated conditions:
  - The Participant Information Leaflet is revised to remove any inconsistencies.
  - All requests for data withdrawals are facilitated, with the exception of data necessary for reporting under the Medical Devices Regulation.
  - Proposed data processing and sharing is clearly outlined in the Participant Information Leaflet and Informed Consent Form.

22-NREC-MD-039-SM2

- Principal Investigator: Prof. Gerry O'Sullivan
- Study title: Gore VIAFORT Vascular Stent VNS 21-05.
- Lead institution: University Hospital Galway, Galway.
- Sponsor: W. L. Gore & Associates B.V.
- NREC-MD Decision
  - *Favourable*

24-NREC-MD-008

- Principal Investigator: Prof. Ivan Casserly
- Study title: Prospective, Single-arm Study to Assess the Safety and Performance of the Omega™ Left Atrial Appendage (LAA) Occluder in Patients with Non-Valvular Atrial Fibrillation and High Bleeding Risk Prospective, Single-arm Study to Assess the Safety and Performance of the Omega™ Left Atrial Appendage (LAA) Occluder in Patients with Non-Valvular Atrial Fibrillation and High Bleeding Risk.
- Lead institution: Mater Private Network, Dublin.
- Sponsor: Eclipse Medical Ltd.
- NREC-MD Decision
  - *Favourable with conditions*
- Associated conditions:

- In line with best practice, study related procedures to be separated from routine clinical procedures as much as practical.
- In relation to participant recruitment and consent, to minimise the potential for perception of coercion, participants to be approached by a suitably qualified member of the study team, who is not involved in routine care for the prospective participant.
- All study related costs to be covered by the sponsor.
- In relation to the Participant Information leaflet, alternative treatment options presented on page 8 of the document to be clearly presented in the first page of the document.

24-NREC-MD-012

- Principal Investigator: Dr Janusz Krawczyk
- Study title: Prospective, Single-arm Study to Assess the Safety and Performance of the Omega™ Left Atrial Appendage (LAA) Occluder in Patients with Non-Valvular Atrial Fibrillation and High Bleeding Risk Prospective, Single-arm Study to Assess the Safety and Performance of the Omega™ Left Atrial Appendage (LAA) Occluder in Patients with Non-Valvular Atrial Fibrillation and High Bleeding Risk.
- Lead institution: University Hospital Galway, Galway.
- Sponsor: Becton, Dickinson and Company – Biosciences
- NREC-MD Decision
  - *Favourable with conditions*
- Associated conditions:
  - Given the rationale provided for mastectomy being an exclusion for peripheral blood sample donation, the same exclusion criteria to be applied for bone marrow donation.
  - Information about the impact of repeated bone marrow donation to be included in the Participant Information Leaflet.

24-NREC-MD-013

- Principal Investigator: Prof. Jarushka Naidoo
- Study title: DIAGNOSTIC DEVICE CLINICAL STUDY PROTOCOL, Performance of VENTANA PD-L1 (SP263) CDx Assay with OptiView DAB IHC Detection on the BenchMark ULTRA Instrument to Determine the PDL1 Expression Level of Non Small-Cell Lung Cancer (NSCLC) Specimens for Roche Phase III Study GO45006.
- Lead institution: Beaumont Hospital, Dublin.
- Sponsor: F.Hoffmann-La Roche Ltd
- NREC-MD Decision
  - *Favourable with conditions*
- Associated conditions:

- The pre-screening PIL/ICF is revised extensively to minimise technical terminology to ensure accessibility.
- The pre-screening PIL/ICF is revised to clearly state that in regards to the “optional” biomarker studies, that these are (a) optional (b) genetic studies and (c) participants will be asked to sign a separate consent form for this. A copy of the biomarker consent form is to be provided to the National Office.
- The information on the risks of false positives in the pre-screening PIL/ICF is revised to clearly state that there are potential side effects from investigational drug if a participant is exposed to the IMP as a result of a false positive. These are currently included in in detail the main CTIMP PIL/ICF, however the NREC-MD requests these are also included in the pre-screening PIL/ICF.

24-NREC-MD-002-SM1

- Principal Investigator: Dr Karen Cadoo
- Study title: Diagnostic Protocol for VENTANA FOLR1 (FOLR1-2.1) CDx Assay for ImmunoGen Study IMGN853-0421 IVD device manufacturer contact information.
- Lead institution: St James's Hospital, Dublin.
- Sponsor: Immunogen Inc.
- NREC-MD Decision
  - *Favourable*

23-NREC-MD-016-SM1

- Principal Investigator: Prof. Robert Byrne
- Study title: Ultimaster Nagomi Sirolimus Eluting Coronary Stent System in Complex Percutaneous Coronary Interventions (PCI) Patients (Nagomi Complex study).
- Lead institution: Mater Private Network, Dublin.
- Sponsor: Terumo Europe N.V.
- NREC-MD Decision
  - *Favourable*

AOB

- The Deputy Chairperson thanked the outgoing members Prof. Anne Parle-McDermott, Prof. Susan O’Connell and Ms Riona Tumelty for their commitment to the Committee over the last three years.
- The Committee agreed to hold a regular meeting in December and instead to take a break in August.
- Dr Lucia Prihodova provided an update on :
  - NREC-MD application management system and forms.

- Quarterly HPRA and NREC meeting.
- guidance documents and policies recently developed:
  - NREC Guidance note - age of consent
  - NREC Guidance note - legally designated representative
  - NREC appeals policy
- The COMBINE project report

- The Deputy Chairperson thanked the Committee and closed the meeting.