NATIONAL OFFICE FOR RESEARCH ETHICS COMMITTEES

National Research Ethics Committee

NREC-MD Meeting Minutes

20th July 2023

Attendance

Name	Role
Prof. Barry O'Sullivan	Chair, NREC-MD
Prof. Mary Sharp	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
Mr Billy McCann	Member, NREC-MD
Dr Sarah McLoughlin	Member, NREC-MD
Prof. Tom Melvin	Member, NREC-MD
Dr Declan O'Callaghan	Member, NREC-MD
Dr Clare O'Connor	Member, NREC-MD
Mr Damien Owens	Member, NREC-MD
Prof. Anne Parle McDermott	Member, NREC-MD
Ms Riona Tumelty	Member, NREC-MD
Prof. Mahendra Varma	Member, NREC-MD
Chita Murray*	Programme Manager, National Office for Research Ethics Committees
Megan O'Neill	Project Officer, National Office for Research Ethics Committees

Dr Emily Vereker	Head, National Office for Research Ethics Committees

*Drafted minutes

Apologies: Prof. Declan Patton (Deputy Chair), Dr Caitriona Cahir, Dr Owen Doody., Dr Gloria Kirwan, Prof. Therese Murphy, Prof. Susan O'Connell, Dr Paul O'Connor, Mr Peter Woulfe

Quorum for decisions: Yes

Agenda

- Welcome (Chairperson)
- Report on Committee business
- Minutes of previous meeting
- Declarations of interest
- 23-NREC-MD-015-R1
- 23-NREC-MD-016-R1
- 23-NREC-MD-017-R1
- 23-NREC-MD-018-R1
- 23-NREC-MD-022
- 23-NREC-MD-023
- 23-NREC-MD-024
- 23-NREC-MD-025
- 23-NREC-MD-010-SM1
- 22-NREC-MD-038-SM1
- 21-NREC-MD-015-SM2
- AOB

- The Chairperson welcomed the Committee, acknowledged apologies sent by applicable members and opened the meeting.
- NREC Committee Business Report: The Committee noted the report.
- Minutes of the previous meeting (15th June 2023) were approved.
- Matters arising from the previous meeting: none
- Declarations of interest:

- Prof. Tom Melvin (23-NREC-MD-016). Prof. Tom Melvin left the meeting for the review of 23-NREC-MD-016
- Dr Sarah McLoughlin (23-NREC-MD-022). Dr Sarah McLoughlin left the meeting for the review of 23-NREC-MD-022.
- Prof. Tom Melvin (21-NREC-MD-015-SM2). Prof. Tom Melvin left the meeting for the review of 21-NREC-MD-015-SM2.

Applications

23-NREC-MD-015

- Principal Investigator: Prof. Jarushka Naidoo
- Study title: Diagnostic Protocol for VENTANA PD-L1 (SP263) CDx Assay in Arcus Biosciences Study ARC-10
- Lead institution: Beaumont Hospital, Beaumont Road, Dublin 9, Ireland
- NREC-MD decision:
  - *Favourable with conditions*
- Associated conditions:
  - Please ensure that the patient information leaflets provide sufficient clarity with regard to the following:
    - The management of tissue samples in the event that an individual withdraws from the study, and any actions required on their part.
    - That participants may be required to forgo existing medications and therapies, and the associated risks.
- In addition, please clarify the following:
  - Whether the PDL1 level of expression is assessed as a front-line diagnostic for standard care in patients with newly diagnosed non-small cell lung cancer (NSCLC), regardless of participation in this study.
  - The system used to evaluate this level of expression in standard of care i.e. VENTANA PD-L1 (SP263) assay or other.
  - That the screening study is not proposed for patients in which PDL1 level of expression has been established in standard diagnosis to be less than 50% TC (with approved companion Dx).

23-NREC-MD-016

- Principal Investigator: Prof. Robert A. Byrne
- Study title: Ultimaster Nagomi Sirolimus Eluting Coronary Stent System in Complex Percutaneous Coronary Interventions (PCI) Patients (Nagomi Complex study)
- Lead institution: Mater Private, Eccles Street, Dublin 7, Ireland

- NREC-MD decision:
  - *Favourable*

23-NREC-MD-017

- Principal Investigator: Prof. Darren Mylotte
- Study title: TRIal to Evaluate TraNsvenous TrIcuspid Valve ReplacemenTwith LuX-Valve Plus System in Patients with Severe or Greater Tricuspid Regurgitation - SafetYand Clinical Performance
- Lead institution: University Hospital Galway, Newcastle Rd, Galway, Ireland
- NREC-MD decision:
  - *Favourable*

23-NREC-MD-018

- Principal Investigator: Prof. Ken McDonald
- Study title: First In Human Clinical Investigation of the FIRE1™ System in Heart Failure Patients
- Lead institution: St. Vincent's University Hospital, Elm Park, Dublin 4, Ireland
- Comments:
  - A request by the Sponsor to edit meeting minutes arising from the NREC-MD meeting of 15 Jun 2023, pertaining to application 23-NREC-MD-018, was not upheld by the Committee.
- NREC-MD decision:
  - *Favourable with conditions*
- Associated conditions:
  - The Participant Information Leaflet is updated to make it explicitly clear to participants that there will be no benefit from participation in the study.
  - Participants should be made aware of the previous version of the implant. Please update the Participant Information Leaflet to inform participants about the Gen1 iteration of this device, and that they will be treated with Gen2.
  - ‘Patient recruitment’ videos which contain suggestive statements are not used for recruitment.

23-NREC-MD-022

- Principal Investigator: Prof. Bryan Hennessy
- Study title: Single arm phase 2 trial of neoadjuvant trastuzumab deruxtecan (T-DXd) with response-directed definitive therapy in early stage HER2-positive breast cancer: a standard chemotherapy-sparing approach to curative-intent treatment (SHAMROCK)

- Lead institution: Beaumont Hospital, Beaumont Road, Dublin 9, Ireland
- NREC-MD decision:
  - *Favourable with conditions*
- Associated conditions:
  - The Patient Information Leaflet is changed to include a statement that potential participants will have a minimum of 24 hours to decide whether to partake in the study.
  - The applicable insurance polic(ies) are extended as necessary for the duration of the study.

23-NREC-MD-023

- Principal Investigator: Dr Dearbhaile Collins
- Study title: Clinical Performance Study Plan for FoundationOne CDX (F1CDx) used as a Clinical Trial Assay (CTA) in the Clinical Trial XPORT-EC-042 for Karyopharm Therapeutics Inc.
- Lead institution: Cork University Hospital, Wilton, Cork, Ireland
- NREC-MD decision:
  - *Favourable with conditions*
- Associated conditions:
  - NREC-MD Application Form:
    - Please confirm to the National Office the number of participants who will take part in the pre-screening F1CDx procedure in order to recruit ten (10) participants in the Rep. of Ireland.
    - In the event that the study seeks to enrol a participant who requires a translated PIL-ICF, translations must be completed by a certified translation provider, and translation certificates submitted to the NREC in advance of distribution of translated documents.
  - Pre-screening PIL and Informed Consent Form (PIL-ICF):
    - Please allow participants 24 hours to consider their participation.
    - Please refer, as applicable, to the risks of a false negative/false positive result as an outcome of pre-screening testing.
    - Please make reference to the protection of data as per the applicable regulations/legislation (GDPR and the Rep. of Ireland).
    - Please outline clearly in the pre-screening PIL-ICF whether individuals may participate in the study if they do not agree to storage of samples.
    - Please include tick boxes for each individual consent item.

    - Please add a separate consent item for the transfer of pseudonymised data outside of the EU.
    - The NREC-MD noted that the PIL-ICF appears to seek blanket consent for future use of samples/data, for unspecified research, without further consent. This type of consent is not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), in which informed consent is a mandatory safeguard. The Committee requests that i) consent is obtained where future use of samples and data is defined such that participants are fully informed, ii) consent for future use of samples should be unbundled (separated and made optional), such that participants may decline the retention of samples but may still participate in the study and/or iii) an option is provided to enable participants to consent to be contacted to provide fresh consent to future research.
- Insurance:
    - Ensure that the validity of applicable insurance policies is maintained for the duration of the study including renewal, inclusive of applicable sites etc.

23-NREC-MD-024

- Principal Investigator: Prof. Gabor Szeplaki
- Study title: Luma Vision's feasibility study on the VERAFEYE system (LUMINIZE)
- Lead institution: Mater Private, Eccles Street, Dublin 7, Ireland
- NREC-MD Decision
    - *Request for further information*
- Further information requested
    - NREC-MD Application Form: The NREC-MD noted that this document requires additional information/amendments. The Committee requests that a revised copy be submitted, with updates at applicable sections:
        - Please confirm the number and name of sites in the Republic of Ireland currently proposed for inclusion in the study, and whether additional sites may be included in due course.
        - Please provide evidence of the applicable pre-clinical studies referred to in the application.
        - The NREC-MD noted that participants will be followed until approximately seven (7) days post procedure, for safety purposes. The Committee requests clarification with regard to the management of medical issues for participants who have been discharged from hospital. In addition, the Committee noted that the post-procedure clinical research form (CRF) states that pulse and blood pressure will be assessed at seven (7) days, and seeks clarification with regard to the conduct of monitoring for participants who may be at home.
        - Please provide applicable evidence and/or justification to support the inference that the VERAFEYE System offers unique benefits.
        - The NREC-MD noted that the study proposes a highly specialised investigation and treatment strategy. The Committee suggests that recruitment and consenting

of participants be performed by an appropriately qualified member of the investigating team (as per MDR) who is an authorised designee of the PI (as per ISO 14155:2020).
    - Please note that, if at any time the investigating team seeks to enrol participants for whom a translated PIL/ICF is required, translation certificates must be submitted to the NREC as a non-substantial amendment prior to distribution of the translated material.
    - Please clarify whether another form of data (e.g. electronic) will be collected, in addition and separate to the paper CRFs, and how imaging data will be transmitted. Please complete all applicable sections of the application form.
    - Please complete the applicable sections of the application form, with regard to the use of radiation.
- Patient Information Leaflet-Informed Consent Form (PIL-ICF): The NREC-MD noted that this document requires additional information/amendments. The Committee requests that a revised copy be submitted, with updates at applicable sections:
    - Please simplify and/or explain medical/technical terminology used throughout the document, including the list(s) of potential risks.
    - Please state that prospective participants will be given a minimum of 24 hours to consider their decision to participate.
    - With regard to the data protection rights of participants, please replace contact detail for the NREC with contact details of the Office of the Data Protection Commissioner.
    - Pseudonymisation of data has been described in the PIL (and NREC-MD application form), not anonymisation (as per the line item in the ICF); please amend this page.
- Insurance:
    - The NREC-MD seeks assurance that applicable insurance polic(ies) will be extended as necessary for the duration of the study, and will include all participants who may be recruited in the Rep. of Ireland.
- Financial Arrangements:
    - The NREC-MD noted that the financial statement provided does not include payment to the Principal Investigator (PI). The Committee requests confirmation whether there is a financial incentive for the PI with regard to patient recruitment.

23-NREC-MD-025

- Principal Investigator: Dr. Janusz Krawczyk
- Study title: Collection and Processing of Bone Marrow (BM) Specimens from healthy volunteers for Analytical Performance Evaluation of the BD Reagent Panels and Kits on the BD Flow Cytometer Systems
- Lead institution: University Hospital Galway, Newcastle Rd, Galway, Ireland
- NREC-MD Decision
    - *Request for further information*

- Further information requested
  - Patient Information Leaflet-Informed Consent Form (PIL/ICF): The NREC-MD noted that this document requires additional information/amendments. The Committee requests that a revised copy be submitted, with updates at applicable sections:
    - With regard to the below statement, please comment on the nature of the results to be communicated to participants, how this will be managed, and whether the participant's general practitioner (GP) will be informed. Please note that clinically significant results must be validated appropriately, and communicated to participants via the appropriate channels with applicable support structure(s) in place.
      - "For the screening laboratory testing, performed by the Clinical Research Facility – University of Galway to assess your eligibility for study participation, if results indicate a virus infection or other clinically significant results, you will get informed about these results".
    - As per the performance study plan, pain medications may be provided. Please update the PIL to reflect this mitigation of risk and to inform the participant of the availability of pain medication/prescription.
    - Documents submitted with the application suggest a median recovery period for participants of twenty (20) days following the bone marrow collection procedure. Please include reference to this duration in the PIL.
    - Please include a diagram (e.g. at section '3. What will happen if you take part in the study?) to illustrate for participants the procedure of bone marrow collection, the applicable area of the body etc. Consider also including a timeline, if more than one visit to site(s) is required.
    - The Committee requests that the applicant outlines clearly whether the blood screening and bone marrow collection will take place in one (1) day (or on separate days), and the location where each procedure will take place. If two (2) visits are required, please include in the advertisement poster.
    - The following statement implies that leftover samples of bone marrow will be destroyed. Please confirm whether blood samples will also be destroyed, and include this information in the PIL: "The bone marrow samples will exclusively be used for this study. Any remnant material will be destroyed after the completion of the study".
    - Please ensure that the PIL clearly outlines where a participant should seek assistance in the event of adverse events following the bone marrow collection e.g. consult their doctor, visit a hospital, visit the research centre etc.
    - Please confirm the role of personnel referred to in the PIL who do not appear to be referred to elsewhere in the submitted documents.
    - Please add tick boxes for each consent item.
    - Please delete reference to illness as participants will be healthy volunteers.
    - The ICF implies blanket consent to future research which contradicts the *specified* future/further research (as required by the Health Research Regulations 2018) which has been outlined in the main body of the PIL. Please amend the ICF accordingly.
  - NREC-MD Application Form: The NREC-MD noted that this document requires additional information/amendments. The Committee requests that a revised copy be submitted, with updates at applicable sections:
    - Please also include the location of the testing laboratories which are referred to, and the location of data analysis.
    - Please clarify the aims of the study, and separate/stratify them accordingly.
    - As noted above, please confirm whether the blood screening and bone marrow collection procedures will take place on the same day.

- Please include the name and location of the institution at which the data key will be held.
- Please confirm that participants will be consented for both taking of the sample and for use of the sample.

- Clinical Research Facility Non-GMP Tissue Procurement For Research Donor Assessment Form:
  - The NREC-MD requests justification for retention of the Donor Assessment questionnaire for thirty (30) years.
  - The NREC-MD requests justification for retention of blood samples for up to thirty (30) years. Note: this duration does not align with the PIL for this study, which suggest that leftover samples will be destroyed.
  - The Donor Assessment Form states that the results of the blood screening procedure will be retained for thirty (30) years. This duration does not align with the PIL for this study, which indicates data retention of ten (10) years. Please clarify.
  - Please clarify whether blood samples to be retained include both those which passed and those which did not pass the blood screening procedure, and provide justification for retention, as above.
  - The NREC-MD noted the below statement and wishes to express its concern. Firstly, the statement implies blanket consent for future research, which does not comply with the Health Research Regulations (2018) which requires, as a mandatory safeguard, explicit consent for specified future research. Secondly, the Committee has been unable to identify the connection between the study as submitted and future developments with regard to DNA or genetics.
    - "I understand that the sample I give for the above study could be used in the future for the development of diagnostic tests and treatments and commercial products (including DNA or Genetic Developments)"

- Financial Arrangements:
  - The NREC-MD noted that participants will receive compensation for loss of earnings etc. While the Committee does not object to the compensation of participants in this study, it requests justification of the monetary amount which has been selected.
  - Please confirm whether formal agreements including payment are in place for the laboratory testing associated with blood sample screening at University Hospital Galway.

23-NREC-MD-010-SM1

- Principal Investigator: Prof. Darren Mylotte
- Study title: Evolut TM EXPAND TAVR II Pivotal Trial
- Lead institution: University Hospital Galway, Newcastle Rd, Galway, Ireland
- NREC-MD Decision
  - *Favourable*

22-NREC-MD-038-SM1

- 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, Elm Park, Dublin 4, Ireland
- NREC-MD Decision
  - *Favourable*

21-NREC-MD-015-SM2

- Principal Investigator: Prof. Robert A Byrne
- Study title: Fractional Flow Reserve or 3D-Quantitative Coronary-Angiography Based Vessel-FFR
- Lead institution: Mater Private, Eccles Street, Dublin 7, Ireland
- NREC-MD Decision
  - *Favourable*

- AOB:
  - Discussion and agreement that certification of testing laboratories is governed by internationally recognised standards and comes within the remit of applicable regulatory bodies (not the NREC) to verify.
  - ICH-GCP E6 revision (R3) is ongoing, and the National Office will circulate links to available online materials.
  - NREC-MD Application Form has been revised and final changes are pending agreement.
- The Chairperson thanked the Committee and closed the meeting.