National Research Ethics Committee

NREC-MD Meeting Minutes

19 September 2024

Attendance

Name	Role
Prof. Barry O'Sullivan	Chair, NREC-MD*
Prof. Declan Patton (Deputy Chair)	Deputy Chair, NREC-MD
Prof. Mary Sharp (Deputy Chair)	Chair, NREC-MD*
Dr Caitriona Cahir	Member, NREC-MD
Dr Daniel Coakley	Member, NREC-MD
Dr Mireille Crampe	Member, NREC-MD
Dr Ruth Davis	Member, NREC-MD
Dr Owen Doody	Member, NREC-MD
Dr Frank Houghton	Member, NREC-MD
Dr James Gilroy	Member, NREC-MD
Dr Gloria Kirwin	Member, NREC-MD
Dr Cara Martin	Member, NREC-MD
Mr Billy McCann	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
Dr Peter Wolfe	Member, NREC-MD
Ms Simone Walshe	Member, NREC-MD

Dr Louise Houston**	Project Officer, National Office for Research Ethics Committees
Dr Sarah McLoughlin	Programme Officer, National Office for Research Ethics Committees
Dr Lucia Prihodova	Programme Manager, National Office for Research Ethics Committees

* Prof. Barry O'Sullivan and Prof. Mary Sharp shared chairing of the meeting.

Apologies: Dr Ruth Davis, Dr Gloria Kirwin, Ms Orla Lane, Prof. Tom Melvin, Prof. Therese Murphy, Mr Damien Owens, 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-017-R1
6. 24-NREC-MD-020-R1
7. 24-NREC-MD-021
8. 24-NREC-MD-022
9. 24-NREC-MD-023
10. 24-NREC-MD-024
11. 24-NREC-MD-025

12. 22-NREC-MD-036-SM4
13. 22-NREC-MD-039-SM3
14. 22-NREC-MD-016-SM4
15. 23-NREC-MD-030-SM1
16. 24-NREC-MD-011-SM1
17. AOB

- Prof. Mary Sharp welcomed the Committee and acknowledged apologies sent and opened the meeting.
- Declarations of interest: None

Applications

24-NREC-MD-017-R1

- 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
  - *Favourable with Conditions*
- Associated conditions
  - The Participant Information Leaflet / Informed Consent Form (PIL/ICF) to be updated to include the likelihood of false positive and false negative results.
  - The PIL/ICF states “You will be asked to attend St. James’s Hospital (Dublin) to receive these two infusions and for testing after NTLA-3001 infusion up to study day 3”. Confirm the role of St. James’s Hospital in this performance study and clarify whether the St. James’s Hospital is in fact one of the study sites. If yes, a site suitability form with PI details and site PI CV should be provided.
  - The NREC-MD notes that that the responsibility for recruitment is with Intellia Therapeautics and that under the protocol the Principal Investigator is responsible for identifying and recruiting suitable participants. In line with Good Clinical Practice, there should be a clear separation of clinical and research activities as much as reasonably possible to minimise any perception of coercion.

24-NREC-MD-020-R1

- 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:
  - The NREC-MD notes that the study objectives, along with the statistical analysis plan for the study have been extensively amended. In addition, a user feedback form, for staff using the CLASSICA-OR method, has been introduced.
  - Comment on whether given the extensiveness of changes, the current application should be submitted to the committee as an entirely new.
  - Provide a clear outline of the changes along with their justification, while referring to the specific documents.
  - Provide a Participant Information Leaflet and Informed Consent Form for staff involved in the staff survey.

24-NREC-MD-021

- Principal Investigator: Prof. Karen Cadoo
- Study title: Diagnostic (Dx) Protocol Title: Diagnostic Protocol for Use of VENTANA FOLR1 (FOLR1-2.1) CDx Assay in Sutro Biopharma Study STRO-002-GM3
- Lead institution: St. James's Hospital
- Sponsor: Sutro Biopharma, Inc.
- NREC-MD Decision
  - *Request for further information*
- Further information requested:
  - The NREC-MD notes that this is a performance study of a non-CE marked device, not undertaken for the purpose of CE marking. Please provide a justification for this process and comment on any future implications of this decision for when the IMP is being placed on market.
  - The NREC-MD notes that while the protocol evaluates the anticipated risks and benefits of participation in the trial, it does not outline neither the risk of using previous material nor risks associated with new biopsy and requests these are included.
  - 'Diagnostic Protocol for Use of VENTANA FOLR1 (FOLR1-2.1) CDx Assay in Sutro Biopharma Study STRO-002-GM' Page 43-44 states that 'it is recommended that

pathologists undergo refresher training' if they have not assessed slides in over 6 months. The NREC-MD requests that rather than recommendation, this is made a requirement.

- Clarify whether there is a time limit on the use of an archival tissue.
- The NREC-MD notes that the study start date listed in the Application Form Section C5 is 01/07/2024, which has already passed. Also, the NREC-MD noted that in Document 8 Diagnostic Protocol Synopsis, the schedule states the study will start in Q3 2023. Clarify the intended start date of the performance study and update the documents accordingly.
- Clarify if the assay will be performed on samples where FOLR1 expression information is already available.
- The NREC-MD noted that the Benefit Risk Assessment is added to the end of the Investigator's Brochure and that incorrect page numbers are used. Please confirm that this approach has been reviewed and approved by the HPRA.
- There are inconsistencies in the lists of participating site countries in Document 13 List of Participating Sites and Application Form Section C4(b). Please clarify the participating countries, sites and number of participants involved in the performance study, and update the relevant documents.
- Provide information on the purpose and utility of the Bridging study referenced in the Diagnostic Protocol Page 22.

24-NREC-MD-022

- Principal Investigator: Prof. Andrew Sharp
- Study title: "SPYRAL AFFIRM Global Clinical Study of Renal Denervation with the Symplicity Spyral Renal Denervation System in Subjects with Uncontrolled Hypertension (SPYRAL AFFIRM)"
- Lead institution: Mater Misericordiae University Hospital
- Sponsor: Medtronic
- NREC-MD Decision
  - *Request for further information*
- Further information requested:
  - Given the proposed study design (single arm nonrandomised study), please comment on the likelihood of the proposed design to deliver robust evidence on the safety and efficacy of the device in the target population.
  - Overall, throughout the application documentation, there is lack of clarity on study specific vs standard care procedures, benefits and risks. Please clarify:
  - Whether the Symplicity Spyral Renal Denervation System is currently routinely available and used in the Mater Misericordiae University Hospital.

- What are the study related follow up procedures vs standard-of-care follow up procedures.
- Clarify whether data from this study will be also entered into the Global Symplicity Registry.
- Clarify the background and methodological properties such as validity and reliability of the Hypertension Health Survey. The NREC-MD noted that some items in the survey were potentially leading and potentially upsetting to participants, eg “How often does your blood pressure make you feel like a burden to your loved ones?”.
- The NREC-MD notes that the maximum number of scans for this study is 1 for renal angiography and denervation, and 1 for renal CT. However, as repeated imaging may be undertaken if the images cannot be evaluated and the angiogram frequency is 2 for all participants, this is not accurate. Confirm the maximum potential number of scans per study participant and update the documentation accordingly.
- The NREC-MD noted that no Data Monitoring Committee will be in place for this study and instead a Clinical Evaluation Committee will be used for categorisation of clinical events and clinical endpoints in the study. The Committee requests a confirmation that this process is sufficiently safeguarding participants, given the additional procedures involved in the study.
- The NREC-MD notes that site Data Protection Officer (DPO) input is outstanding and requests that their feedback is obtained and implemented prior to initiating the study.
- Confirm if the person(s) undertaking the interview for recruitment and the person(s) conducting the telephone survey are the same. Clarify what qualifications the individual(s) will hold.
- The NREC-MD noted that the provided promotional materials lack in detail and imply that an individual must participate in the study in order to avail of the device. Please revise the promotional materials for transparency.
- The recruitment material should be revised to remove the descriptor ‘important’.
- The recruitment material should be revised to remove the sentence “enrolment is limited”, as this poses a risk of indue influence or a sense of unnecessary urgency to potential participants. More neutral language should be used.
- The PIL/ICF requires additional information/amendments to improve readability and accessibility due to overly technical language not suitable for a layperson (e.g. explain what a CE mark is).
- The PIL/ICF should be updated for transparency to clearly inform potential participants that this device is already on the market and accessible without participating in this study.
- The study involves additional scans that would not be normal standard of care. The PIL/ICF should be updated to clearly inform participants of the additional radiation risk involved in taking part in the study.

- As this device is already CE-marked and available for use in standard care, the PIL/ICF should be updated to clearly outline the benefits of the device within this study rather than the benefits of the device alone.
- The section in the PIL/ICF “What happens if I am injured or hurt during this study?” should be updated to clarify who exactly is responsible for what if an injury occurs as a result of the study.
- The PIL/ICF includes statements which do not fully comply with applicable data protection legislation. The NREC-MD requests an update to the ICF, per the requirements of the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), such 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.

24-NREC-MD-023

- Principal Investigator: Prof. Robert Byrne
- Study title: Randomised trial of dual device treatment involving drug-coated balloon angioplasty and drug-eluting stent implantation compared to single device treatments in patients with diabetes mellitus – the DUBSTENT-DIABETES trial
- Lead institution: Mater Private Network
- Sponsor: Royal College of Surgeons Ireland
- NREC-MD Decision
  - *Request for further information*
- Further information requested:
  - Section J1 of the NREC-MD Application Form states that participants of childbearing potential will be included in this study, however Section J2 indicates differently. Clarify this discrepancy and update the documentation accordingly.
  - Section K9 of the NREC-MD Application Form to be updated to confirm what personal information RCSI will collect.
  - The NREC-MD notes the use of Optical Coherence Tomography in the Protocol. Section O of the NREC-MD Application Form should be updated, as appropriate, for the use of this procedure. The Site Suitability Forms should also be updated as appropriate.
  - The NREC-MD requests confirmation of any additional x-ray exposure outside of standard of care for this study. Section O of the NREC-MD Application Form should be updated as appropriate.

- Section R1 of the NREC-MD Application Form should be updated to confirm funding has been secured for the duration of the study.
- The NREC-MD notes that the proposed study does not include standard of care arm and requests justification for this approach.
- The NREC-MD notes that the devices used in this study incorporate an ancillary medicinal product and requests clarification if this study also falls under the Clinical Trials Regulation and requires review by NREC-CT.
- The NREC-MD notes that study participants will undergo angiography review at 6m post procedure and requests clarification on whether this is part of standard care or study specific procedure.
- As potential participants are consented prior to the index coronary angiography, confirm that all screening required investigations conducted prior to consent are standard care investigations.
- The NREC-MD notes that participants may receive dual antiplatelet therapy for a period of 3-12 months. Please confirm that the dual antiplatelet therapy received by participants for 3 months post sole DCB (Pantera Lux) is considered standard of care.
- The NREC-MD notes the protocol references a prespecified sub-study including 30 patients who will undergo Optical Coherence Tomography. Clarify if this procedure is aligned with standard of care and where relevant include details of this sub-study in the Participant Information Leaflet / Informed Consent Form (PIL/ICF).
- Section 6 of the PIL/ICF “Are there any alternative treatments?” to be updated to make it clear that routine percutaneous interventions are an option apart from those outlined in the study.
- The NREC-MD notes that for participants whose primary language is not English, routine hospital interpreter facilities may be used. Confirm if there are any intentions to provide a translation of the PIL/ICF for such participants?

  The NREC-MD requests that in the event that translated copies of participant-facing documents and services of interpreter are provided for participants for whom English is not their native language, or who do not speak English. Translations must be completed by a certified translation provider, and the translation certificates submitted to the National Office for Research Ethics Committees as a non-substantial modification in advance of the distribution of translated documents.
- The NREC-MD notes that participant data is to be anonymised and shared for future open research and requests specific consent for anonymisation is included in the ICF.
- The NREC-MD requests that section on risks is updated to include their likelihood.
- The financial disclosure forms should be updated and expanded to include:
    - All financial arrangements including hospital costs / visits and other financial arrangements outside of this.
    - Confirmation of what payments are being made to Core Lab and the relationship between Core Lab and the Principal Investigator.

    - Confirmation if Biotronik provides disposables (catheters, DCP, DES etc.) free of charge for the study?
    - Confirmation if the investigational devices are provided free of charge to participants, HSE and insurer where relevant.
- All reasonable participant expenses to be reimbursed, including study related costs for participants attending follow-up visits (e.g. 6-month angiography). All compensation should be outlined in the PIL.

24-NREC-MD-024

- Principal Investigator: Prof. Gerry O'Sullivan
- Study title: Product Surveillance Registry Aortic, Peripheral & Venous (PSR APV)
- Lead institution: University Hospital Galway
- Sponsor: Medtronic
- NREC-MD Decision
    - *Favourable with conditions*
- Associated conditions:
    - Confirm that participants will only be enrolled prior to intervention only if it clear that they may receive a Medtronic eligible product. If it is clear they will not receive an eligible product, unnecessary engagement should be avoided.
    - The PIL/ICF to be updated to remove any typographical errors.
    - The NREC-MD requests that participants are given a minimum 24 hours to review and consider the PIL/ICF before their consent is sought.
    - The Participant Information Leaflet / Informed Consent Form (PIL/ICF) is updated to make it clear that only health-related information relevant to the purposes of this study (i.e. evaluation of the safety and effectiveness of the Abre™ Venous Self-expanding Stent System) will be collected. Reference to non-specific broad category collection of data must be removed (e.g. additional health information as determined by the registry staff or Medtronic).
    - As health information may be collected from the participants family or health-care providers, a specific consent box must be included in the ICF for this.
    - As some participants may not be covered by either the healthcare system or private medical insurance, the PIL/ICF should be updated to make it clear what costs a participant may incur by participating in this study.
    - The line "if you decide to be in this registry you will sign and date this form" on Page 1 of the PIL/ICF to be updated to "…… you will be asked to sign and date this form".
    - Section "Do I have the right to refuse to be in this registry or to leave this registry?" on Page 3 of the PIL/ICF to be reworded to make it clear to the participant that they can

leave the study at any time, without explanation, and it will not affect their current or future care in any way.

- As the doctors and nurses are employees of the hospital and the hospital itself is a data processor, Page 3 of the PIL/ICF “How will be data be processed?” should be updated to clarify this.
- The email address for the DPO on Page 5 of the PIL/ICF to be updated.
- The PIL/ICF to be updated to make it clear that the future research is related to venous products rather than coronary products.
- The PIL/ICF to be revised to define areas of future research more clearly, as the current wording stated on page 4 implies blanket consent which is unlawful:
- The PIL/ICF to clarify that any future research involving data from this study is subject to research ethics committee review.
- As this is an industry sponsored patient registry, the Health Research Board (HRB) logo to be removed from the PIL/ICF.
- Page 6 of the PIL/ICF, as participants may require more than a link to the clinicaltrials.gov website to access the study results, the sponsor must provide a direct access link to participants upon request.
- Page 7 of the PIL/ICF to be updated to clarify exactly how long participant data will be kept for.
- The PIL/ICF to be updated to inform participants that they will be required to complete a ‘patient diary’ at home and bring this to clinical on their 30 day patient visit.
- The Clinical Investigation Agreement to be finalised prior to initiating the study.
- Data Protection Officer (DPO) input to be obtained and implemented prior to initiating the study.

24-NREC-MD-025

- 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
- Sponsor: BillionToOne
- NREC-MD Decision
  - *Favourable with conditions*
- Associated conditions:

- Section G4 of the NREC-MD Application Form to be updated to clarify who a sub-investigator might be and what their qualifications will be.
- The timeline for recruitment, and indeed how and when the recruitment and consenting process will take place, is currently unclear from the presented documentation. Clarify this process in the NREC-MD Application Form.
- Section F7 of the NREC-MD Application Form to be updated to clarify or correct how participants will be identified and selected from the larger trial without access to identifiable information.
- The Participant Information Leaflet / Informed Consent Form (PIL/ICF) is updated to correct all typographical errors.
- Update PIL/ICF (p3) to clarify the inconsistency between the statements "…intended for use at ten (10) weeks or more gestational age" and "During the screening period (week 8 -16 of your pregnancy) …".
- Update Section "What are the benefits of participating in the performance study?" to improve readability and accessibility.
- Update to include information on risks of false positives/ negatives to clearly state
  - the likelihood of false positives/ negatives
  - the risks associated with false negative results and how they will be mitigated (i.e. participant will receive standard of care treatment)
  - the risks associated with false positive results and how they will be mitigated.
- The NREC-MD requests that participants are given a minimum 24 hours to review and consider their participation in the study.
- The PIL is updated to clarify that participants will not receive payment for screening but may receive compensation for reasonable expenses, as per budget allocation.
- The ICF is updated to include explicit and itemised consent for transfer of data and samples outside of the EU to the USA.

22-NREC-MD-036-SM4

- Principal Investigator: Prof. Faisal Sharif
- Study title: A Prospective, Multi-Center, Open-Label, Single-Arm Clinical Trial Evaluating the Safety and Efficacy of the Cordella™ Pulmonary Artery Sensor System in New York Heart Association (NYHA) Class III Heart Failure Patients (PROACTIVE-HF Trial)
- Lead institution: University Hospital Galway
- Sponsor: Endotronix
- NREC-MD Decision
  - *Favourable*

22-NREC-MD-039-SM3

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

22-NREC-MD-016-SM4

- Principal Investigator: Prof. Carel LeRoux
- Study title: "A Prospective, Randomized, Double-Blind, Sham-Controlled, Multi-Center Pivotal Study to Evaluate the Efficacy and Safety of Duodenal Mucosal Resurfacing Using the Revita® System in Subjects with Type 2 Diabetes on Insulin therapy"
- Lead institution: St. Vincent's University Hospital, Dublin
- Sponsor: MWB Consulting SARL
- NREC-MD Decision
  - *Favourable*

23-NREC-MD-030-SM1

- Principal Investigator: Prof. Norman Delanty
- Study title: Wireless Ultra Long-Term EEG recordings in Epilepsy -A prospective long-term clinical evaluation using the UNEEG EpiSight solution
- Lead institution: Beaumont Hospital
- Sponsor: UNEEG medical A/S
- NREC-MD Decision
  - *Favourable with conditions*
- Associated conditions:
  - As visits 4-9 are now in-person only, all reasonable participant expenses must be reimbursed. All compensation should be outlined in the PIL.

24-NREC-MD-011-SM1

- Principal Investigator: Dr Noel Horgan

- Study title: A Phase 3 randomized, masked, controlled trial to evaluate efficacy and safety of belzupacap sarotalocan (AU-011) treatment compared to sham control in subjects with primary indeterminate lesions or small choroidal melanoma
- Lead institution: Royal VictoriaRoyal Victoria Eye and Ear Hospital
- Sponsor: Aura Biosciences
- NREC-MD Decision
  - *Favourable*

AOB

- Dr Lucia Prihodova outlined the plans for upcoming Member forum event in December 2024 and asked that members indicate their attendance.