NATIONAL OFFICE FOR RESEARCH ETHICS COMMITTEES

National Research Ethics Committee

NREC-MD Meeting Minutes

17 November 2022

Attendance

Name	Role
Prof. Barry O'Sullivan	Chairperson, NREC-MD
Prof. Mary Sharp	Deputy Chairperson, NREC-MD
Prof. Declan Patton	Deputy Chairperson, NREC-MD
Dr Mireille Crampe	Member, NREC-MD
Dr Ruth Davis	Member, NREC-MD
Dr Gloria Kirwan	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
Prof. Susan O'Connell	Member, NREC-MD
Dr Clare O'Connor	Member, NREC-MD
Dr Paul O'Connor	Member, NREC-MD
Mr Damien Owens	Member, NREC-MD
Ms Riona Tumelty	Member, NREC-MD

Dr Emily Vereker	Head, National Office for Research Ethics Committees
Dr Lucia Prihodova*	Programme Manager, National Office for Research Ethics Committees
Ms Megan O'Neill	Project Officer, National Office for Research Ethics Committees

*Drafted minutes

Apologies: Dr Caitriona Cahir, Dr Owen Doody, Dr Frank Houghton, Prof. Therese Murphy, Dr Declan O'Callaghan, Dr Catherine O'Neill, Prof Anne Parle McDermott, Prof. Mahendra Varma, Mr Peter Woulfe

Quorum for decisions: Yes

Agenda

1. Welcome
2. Report on Committee business
3. Minutes of previous meeting
4. Declarations of interest

Responses to RFFIs:

5. 22-NREC-MD-034-R1
6. 22-NREC-MD-035-R1

New applications:

7. 22-NREC-MD-036
8. 22-NREC-MD-037
9. 22-NREC-MD-038
10. 22-NREC-MD-039
11. 22-NREC-MD-040

Substantial Amendment applications:

12. 22-NREC-MD-041-SA1
13. 21-NREC-MD-014-SA2
14. 22-NREC-MD-027-SA1

15. AOB

- Prof. Mary Sharp, the Deputy Chairperson welcomed the Committee and opened the meeting.
- NREC Committee Business Report: The Committee *noted* the report.
- Minutes of previous meeting (13 October 2022) & matters arising: The minutes were *approved*.
- Declarations of interest:
    - Prof Declan Patton (22-NREC-MD-034). Prof Patton left the meeting for the review of 22-NREC-MD-034.
    - Dr Catherine O'Neill (22-NREC-MD-034). Dr O'Neill left the meeting for the review of 22-NREC-MD-034.
    - Prof Tom Melvin (22-NREC-MD-034). Prof Melvin left the meeting for the review of 22-NREC-MD-034.
    - Mr Billy McCann (22-NREC-MD-038). Mr McCann left the meeting for the review of 22-NREC-MD-038.
    - Ms Riona Tumelty (22-NREC-MD-037 & 22-NREC-MD-040). Ms Tumelty left the meeting for the review of 22-NREC-MD-037 & 22-NREC-MD-040.
- Prof. Mary Sharp, the Deputy Chairperson, handed over the chairing of the meeting to Prof. Barry O'Sullivan.

Applications

22-NREC-MD-034-R1

- Principal Investigator: Prof. John McDermott
- Study title: Wound Assessment Using Spectral Imaging (WAUSI).
- Lead institution: Connolly Hospital Blanchardstown, Mill Rd, Abbotstown, Dublin, D15 X40D.
- NREC-MD comments
    - The Committee noted that this was a response to request for further information issued following the 13 October 2022 NREC-MD meeting NREC-MD.
- NREC-MD decision
    - *Favourable*

22-NREC-MD-035-R1

- Principal Investigator: Prof. Faisal Sharif
- Study title: Product Surveillance Registry (PSR) Coronary
- Lead institution: Mater Private Network, Eccles St, Dublin 7, D07 WKW8.
- NREC-MD comments
  - The Committee noted that this was a response to request for further information issued following the 13 October 2022 NREC-MD meeting NREC-MD.
- NREC-MD decision
  - *Favourable with conditions*
- Further information requested:
  - A copy of GP letter is provided to the National Office for our records.

22-NREC-MD-036

- 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: NUI Galway and Galway University Hospital, Newcastle Road, Galway, H91 YR71.
- NREC-MD comments
  - The NREC-MD noted that this application is a resubmission of a clinical investigation focused on the Cordella™ Pulmonary Artery Sensor System that previously received an unfavourable decision. The Committee acknowledged the effort put into the revised application and noted that the application documentation is much improved.
- NREC-MD decision
  - *Request for further information*
- Further information requested:
  - The NREC-MD noted the response regarding continued use of the device and requests clarification on any plans to undertake such study in Ireland.
  - In relation to those who elect to continue to use the device for routine care purposes after the end of the study, the NREC-MD requests clarification on supports available and cost to those who chose to avail of this service, whether the study sites agreed to ongoing use of the device for routine care purposes and a clarification on any additional risks, benefits or ethical issues associated with ongoing use of the device for routine care purposes.
  - The NREC-MD requests that following participant withdrawal, the only data collected and reported pertains to data on adverse event required to be reported under the Medical Devices Regulation (EU) 2017/745.

- The NREC-MD requests that participants are allowed minimum 24 hours to consider their participation in the study and that this is reflected in the participant facing documentation.
- The NREC-MD noted that the application pack included a number of promotional and participant facing materials and requests clarification on how and when these documents will be used over the course of the study.
- The NREC-MD requests a clarification on whether the approval of the site Radiation Protection Officer/ Board has been granted for the study.

22-NREC-MD-037

- Principal Investigator: Prof. David Burke
- Study title: A single-centre, investigator-led, observational clinical investigation to evaluate the performance of ECG gathered from a single arm for the detection of heart rhythm abnormalities, as compared to hospital telemetry ECG.
- Lead institution: Beacon Hospital, Sandyford, Dublin 18, D18 AK68.
- NREC-MD comments
  - The NREC-MD noted that this application is a resubmission of a low-risk clinical investigation focused on a biometrics-monitoring armband that previously received an unfavourable decision. The Committee acknowledged the effort put into the revised application and noted that the application documentation is much improved.
- NREC-MD decision
  - *Favourable with conditions*
- Associated conditions
  - The data retention is aligned with the time periods specified in the Medical Device Regulations (EU) 2017/745.
  - The first item of the informed consent form is amended to reflect the actual length of the Participant Information Leaflet and Informed Consent Form.

22-NREC-MD-038

- 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, D04 T6F4.
- NREC-MD comments
  - The Committee noted that this was an application for clinical investigation exploring an artificial intelligence-driven echocardiographic software algorithm in community setting.
- NREC-MD decision

- *Favourable with conditions*

- Associated conditions
  - Informed Consent Form page 2 under 'Storage and future use of information' point 2 is rephrased for accessibility and clarity indicating 1) consent to store data for possible future research and 2) consent to be contacted for the purposes of requesting consent for any future processing of this data in relation to an unrelated study.
  - The Informed Consent Form includes an item seeking explicit consent for the processing of participant personal data outside of the EEA.
  - A review by the site Data Protection Officer of the study DPIA is obtained and that their comments are incorporated before the study proceeds.
  - The NREC-MD noted that the site suitability form refers to "relatively untrained professional" who will carry out the procedure. The Committee requests that:
    - examples of the job title(s) and/or the levels of medical training of such individual(s) are provided in a response to this decision letter
    - Dr Barrett will ensure that necessary training is provided to such individual to carry out all necessary study procedures.

22-NREC-MD-039

- Principal Investigator: Mr Gerry O'Sullivan
- Study title: Wound Assessment Using Spectral Imaging (WAUSI).
- Lead institution: NUI Galway and Galway University Hospital, Newcastle Road, Galway, H91 YR71.
- NREC-MD comments
  - The NREC-MD noted that this application is a resubmission of a first in human clinical investigation focused on vascular stent for treatment of symptomatic inferior vena cava obstruction that previously received an unfavourable decision. The Committee acknowledged the effort put into the revised application and noted that the application documentation is much improved.
- NREC-MD decision
  - *Favourable with conditions*
- Associated conditions
  - Section 5.4 of the Clinical Investigation Plan is updated to align with the consent procedure described in the cover letter provided.
  - The language in the ICF (Page 2, point 2) is updated to make it clear that the participant's pseudonymised personal data may only be used in future research in an area related to this study.
  - The NREC-MD appreciates follow up visits have been included at additional points. However, given that this is the first in human study, the Committee encourages the

Applicant considers implementing more frequent patient follow-up visits over the first-year post procedure.

- Participants are reimbursed for all reasonable expenses associated with their participation in the study.
- Item 2 on page 2 of the Informed Consent Form relating to future use of data is revised for clarity reflecting that the future medical research purposes and studies are limited to the area of iliocaval venous disease and the development of the study device as described in the Participant Information Leaflet. In line with best practice, the NREC-MD requests to separate the consent for the two categories of future research.
- Item 11 on page 2 of the Informed Consent Form is removed as applicants have confirmed that study participation will not be charged for their participation.

22-NREC-MD-040

- Principal Investigator: Prof. Sean Kennelly
- Study title: Blood-based biomarker pre-screening and CSF testing with immunoassays for the SKYLINE Phase III study.
- Lead institution: Tallaght University Hospital, Tallaght, Dublin 24, D24 NR0A.
- NREC-MD comments
  - The NREC-MD noted that this application is an application for performance study of an in vitro diagnostic medical device in participants at risk of Alzheimer's disease.
- NREC-MD decision
  - *Request for further information*
- Further information requested:
  - The NREC-MD noted that the application documentation was unnecessarily complex and using technical language, including the lay sections of the application form.
  - The NREC-MD noted that at times it was difficult to distinguish whether the information/ documentation provided related to the performance study (PS) or the associated clinical trial of investigative medicinal product (CTIMP).
  - Furthermore, the NREC-MD noted that a number of documents relating to the CTIMP were included in the submission, eg the main study protocol and ICF. The Committee acknowledges the interlink between the PS and CTIMP. To ensure clarity, the Committee requests that specific documentation for each is provided/ sections relevant to the PS are highlighted in the documentation, eg the DPIA, main study protocol, ICF.
  - The Committee requests a clarification on the scientific justification of the PS, and how will the information generated by the PS used in the context of the current CTIMP and potentially in the context of wider research and clinical practice.

- The NREC-MD noted that the document 6_WN42444 Prescreening ICF_IE V2.0_08Sep22 based on Global Version 1 dated 24Sep2021_TC.docx includes consent items on genetic data, however neither the PIL nor the protocol for the performance study provide any information on type of genetic data collected as a part of the study and its proposed processing.
- The NREC-MD noted that no justification for the genetic data being collected as the study relevant information can be identified via plasma, blood and the cerebral spinal fluid.
- Furthermore, the Committee requests that if any of the samples collected as a part of the PS are to undergo genetic testing, section M of the application form must be completed and the information must be included in the PIL and protocol. Alternatively, if no genetic data is being collected and processed as a part of the PS, the relevant forms must be amended accordingly.
- The NREC-MD noted that the study aims to recruit participants with normal cognition and family history through memory clinics, Ireland's Alzheimer's Café network and other collaborative networks. The NREC-MD requests a clarification on potential vulnerability of such prospective participants, and potential selection bias of the proposed recruitment strategy and any steps taken to mitigate its impact.
- The NREC-MD requests a clarification on the assessment of capacity as a part of the PS and implications in changes in capacity for participants.
- The NREC-MD noted that the provided Participant Information Leaflets/ Informed Consent Form is very long and utilises technical terminology and requests it is revised to improve accessibility of the document for prospective participants.
- The NREC-MD noted that page 5 of document 6_WN42444 Prescreening ICF_IE V2.0_08Sep22 refers to "stopping safely". The Committee requests clarification on any risks associated with withdrawal from the PS and that the language is amended to more neutral tone.
- The NREC-MD requests that withdrawal of consent from the study is also indicated as a withdrawal of samples.
- Additionally, the NREC-MD requests that the consent form is revised to facilitate truly unbundled consent.
- The NREC-MD noted that the data processing details are provided after the consent forms and requests this section is revised for accessibility and outlined before participant consent is sought.
- The NREC-MD noted that document 6_WN42444 Prescreening ICF_IE V2.0_08Sep22 refers participants to the NREC-MD if they have any question about their rights. The Committee requests this is removed and that participants are directed to relevant study team member instead.
- The NREC-MD noted inconsistencies in the application documentation on the location of the sample processing, ie site or elsewhere and requests clarification.

22-NREC-MD-041-SA1

- Principal Investigator: Prof. Carel Le Roux
- Study title: A randomized, double blind sham controlled clinical trial to evaluate the efficacy of vestibular nerve stimulation (VeNS), together with a lifestyle modification programme, compared to a sham control with a lifestyle modification programme, as a means of improving glycemic control in adults with type 2 diabetes mellitus – Substantial Amendment.
- Lead institution: St Vincent's University Hospital, Elm Park, Dublin 4, D04 T6F4.
- NREC-MD comments
  - The NREC-MD noted that this application is a substantial amendment application for a study previously approved by the SVUH REC and that The NREC-MD noted that this application includes a number of different amendments and that majority of them are justifiable and reasonable.
- NREC-MD decision
  - *Request for further information*
- Further information requested:
  - The NREC-MD noted the changes to protocol intended to improve recruitment by changing the threshold of the blood sugar and BMI, and that participants will be given different dietary advice depending on their BMI.
  - The Committee noted that this approach potentially introduces a fatal flaw in the study as it effectively creates two different study groups with two different protocols. The Committee noted that the effect of the of device combined with lifestyle programme is likely to vary across the groups, potentially leading to difficulties in interpreting data on the effectiveness of the device, and that this issue is not addressed in the submitted study protocol and analysis plan.
  - To that end, the Committee requests a justification for this approach and clarification on how it will the challenges presented by the change in protocol be mitigated in terms of analyses and interpretation of results.
  - Alternatively, the Committee requests that alternative options to improve recruitment are considered, along with the need to introduce dietary advice at all.
  - The NREC-MD noted that participation in the study poses a significant commitment from the participants and requests that due consideration is given is to whether the proposed amendment will further impact participant recruitment.
  - Finally, the NREC-MD asks that a due consideration is given to the need to introduce a DMC or a steering committee to the trial, as an added safeguarding measure for both participants and the study team.

21-NREC-MD-014-SA2

- Principal Investigator: Dr Martin Buckley

- Study title: Randomised, single dose, crossover, open label, placebo controlled, single site confirmatory clinical investigation in patients with gastro-oesophageal reflux, to characterise the acid neutralisation activity of a calcite chewing gum, using oesophageal ambulatory pH monitoring.
- Lead institution: Mercy University Hospital, Grenville Place, Centre, Cork, T12 WE28.
- NREC-MD comments
  - The NREC-MD noted that this is an application for substantial amendment. In this regard, the NREC-MD opinion pertains only to the substantial amendment of:
    - The revised inclusion criterion from “patient is aged: ≥ 18 years ≤ 60 years” to “patient is aged: ≥ 18 years ≤ 70 years”, reflected in the Clinical Investigation Plan and Patient Invitation Letter.
    - The projected patient 'drop-out' rate changed from 20% to 10%.
    - As a result of the updated patient 'drop-out' rate, the number of participants required for randomisation in the study has been revised to 27.
- NREC-MD decision
  - *Favourable with conditions*
- Associated conditions
  - The NREC-MD noted that the Participant Information Leaflet and Informed Consent Form refer to COVID-19 on page 8. The Committee encourage that consideration is given to adding an additional comment regarding the increased risks of COVID-19 to the older participants of the study.

21-NREC-MD-027-SA1

- Principal Investigator: Prof. Richard Costello
- Study title: CONNected Electronic Inhalers Asthma Control Trial 3 (CONNECT 3), a 24-Week Treatment, Multicenter, Open-Label, Randomized, Parallel Group Comparison Study of Standard of Care Treatment Versus the Budesonide/Formoterol Digihaler Digital System, to Optimize Outcomes in Adult Patients with Asthma.
- Lead institution: Beaumont Hospital, Beaumont Rd, Dublin 9, D09V 2N0.
- NREC-MD comments
  - The NREC-MD noted that this is an application for substantial amendment. In this regard, the NREC-MD opinion pertains only to the substantial amendment of:
    - The role of gatekeeper
    - Continued inclusion of participants who become pregnant while enrolled in the study
- NREC-MD decision
  - *Favourable with conditions*
- Associated conditions

- The NREC-MD noted the logistic challenges in identifying a gatekeeper in each site. To that end, the Committee noted that such role can be completed by a study team member, independent of the care team for such participants, who is not necessarily site based, ie one gatekeeper for study rather than each site. In this particular study, the gatekeeper would assist prospective participants in the review of the Participant Information Leaflet and deciding on whether or not they wish to participate in the study. As this is a combinational study, to ensure compliance with SI 190/2004, the PI then oversees the recording of the consent.
- Participants who become pregnant over the course of the study are offered an opportunity to discuss their continued participation in the study with a gatekeeper to further safeguard their right to independently consider their decision to progress or withdraw from the study.

AOB

- Dr Lucia Prihodova, the Programme Manager noted that an additional meeting will be held in December to review the responses to requests for further information issued at the current meeting.
- The Chairperson thanked the Committee and closed the meeting.

NREC-MD Meeting Minutes

15 December 2022

Attendance

Name	Role
Prof. Barry O'Sullivan	Chairperson, NREC-MD
Prof. Mary Sharp	Deputy Chairperson, NREC-MD
Prof. Declan Patton	Deputy Chairperson, NREC-MD
Dr Mireille Crampe	Member, NREC-MD
Dr Ruth Davis	Member, NREC-MD
Dr Frank Houghton	Member, NREC-MD
Dr Gloria Kirwan	Member, NREC-MD
Mr Billy McCann	Member, NREC-MD
Dr Sarah McLoughlin	Member, NREC-MD
Prof. Tom Melvin	Member, NREC-MD
Dr Lucia Prihodova*	Programme Manager, National Office for Research Ethics Committees
Ms Megan O'Neill	Project Officer, National Office for Research Ethics Committees
Dr Emily Vereker	Head, National Office for Research Ethics Committees

*Drafted minutes

Apologies: Dr Caitriona Cahir, Dr Owen Doody, Ms Orla Lane, Prof. Therese Murphy, Dr Declan O'Callaghan, Prof. Susan O'Connell, Dr Clare O'Connor, Dr Paul O'Connor, Dr Catherine O'Neill, Mr Damien Owens, Prof Anne Parle McDermott, Ms Riona Tumelty, Prof. Mahendra Varma, Mr Peter Woulfe

Quorum for decisions: Yes

Agenda

1. Welcome

2. Matters arising
3. Declarations of interest

Responses to RFFIs:

4. 22-NREC-MD-036-R1
5. 22-NREC-MD-041-SA1-R1

Substantial Amendment applications:

6. 22-NREC-MD-005-SA1

7. AOB

- Prof. Barry O'Sullivan, the Chairperson, welcomed the Committee and opened the meeting.
- Matters arising: the NREC-MD noted that application 22-NREC-MD-040 was withdrawn due to termination of the performance study.
- Declarations of interest: none.

Applications

22-NREC-MD-036-R1

- 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: NUI Galway and Galway University Hospital, Newcastle Road, Galway, H91 YR71.
- NREC-MD comments
  - The Committee noted that this was a response to request for further information issued following the 17 November 2022 NREC-MD meeting NREC-MD.
- NREC-MD decision
  - *Favourable with conditions*
- Associated conditions
  - Page 9 of document 4.3 ML1273 Rev 2_PROACTIVE-HF Flip Chart is removed and is not used with participants during the decision-making or consenting process, as the

NREC-MD noted the phrasing as overly promotional. The Committee also noted, that the study gatekeeper should cover the contents of the full participant information leaflet when outlining the study to prospective participants, rather than relying on the PROACTIVE-HF Flip Chart document.

22-NREC-MD-041-SA1-R1

- Principal Investigator: Prof. Carel Le Roux
- Study title: A randomized, double blind sham controlled clinical trial to evaluate the efficacy of vestibular nerve stimulation (VeNS), together with a lifestyle modification programme, compared to a sham control with a lifestyle modification programme, as a means of improving glycemic control in adults with type 2 diabetes mellitus – Substantial Amendment.
- Lead institution: St Vincent's University Hospital, Elm Park, Dublin 4, D04 T6F4.
- NREC-MD comments
  - The Committee noted that the response from the Applicant addressed majority of the queries raised by the Committee.
  - However, the response did not address the query pertaining to the introduction of a new participant subgroups by changing the threshold of the blood sugar and BMI. As per the initial NREC-MD letter, the Committee queried whether introduction of different dietary advice depending on participant's BMI will be effectively creating two different study subgroups with two different protocols.
  - The NREC-MD noted that the response neither addressed the impact of this change on the interpretability of the study results, nor appeared to be reflected in the statistical analysis plan. There is no reference to the differences introduced by the proposed amendment whereby those with <25 BMI will not be requested to undertake a 500 kcal deficit but those with BMI >25 will be. The subgroup analysis in this statistical analysis plan does not appear to take into account the additional subgroup of caloric restriction that the proposed amendment will create.
  - The response therefore did not address the ethical issue of participants potentially taking part in a study that may not have a sufficient robustness.
  - Finally, the NREC-MD further noted that no information was provided on if or how will the issue of the study subgroups be reported in any scientific publications and regulatory reports generated at the end of the study.
- NREC-MD decision
  - *Unfavourable*

22-NREC-MD-005-SA1

- Principal Investigator: Dr Jonathan Lyne
- Study title: Conduction System Pacing Optimized Therapy (CSPOT) – Substantial amendment.

- Lead institution: Beacon Hospital, Sandyford, Dublin 18, D18 AK68.
- NREC-MD comments
    - The NREC-MD noted that this is an application for substantial amendment. In this regard, the NREC-MD opinion pertains only to the substantial amendment of:

    1. The safety of the subjects: improves safety by allowing more flexibility to Investigators to choose best CSPOT configuration in case of phrenic nerve stimulation, lead dislodgement or high capture threshold.
    2. Study data reliability: Statistical Design and Methods section has been updated for clarification; main change was to replace “mean SDAT” with “Improvement in SDAT relative to baseline” in the hypotheses.
    3. The conduct of the study: additional flexibility for Investigators at the end of the acute protocol.
    4. The safety of device used in the study: safety improved by allowing the Investigators to “deviate” from optimal configuration if more beneficial for patient.

- NREC-MD decision
    - *Favourable*

AOB

- The Chairperson thanked the Committee and closed the meeting.