NATIONAL OFFICE FOR RESEARCH ETHICS COMMITTEES

National Research Ethics Committee

NREC-MD Meeting Minutes

19 January 2023

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 Owen Doody	Member, NREC-MD
Dr Frank Houghton	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
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

Name	Role
Mr Damien Owens	Member, NREC-MD
Ms Riona Tumelty	Member, NREC-MD
Mr Peter Woulfe	Member, NREC-MD
Dr Lucia Prihodova	Programme Manager, National Office for Research Ethics Committees
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: Dr Caitriona Cahir, Dr Catherine O'Neill, Prof Anne Parle McDermott, Prof. Mahendra Varma

Quorum for decisions: Yes

Agenda

- Welcome (Chairperson)
- Presentation from the Medical Devices team of the HPRA
- Report on Committee business
- Minutes of previous meeting
- Declarations of interest
- 23-NREC-MD-001
- 23-NREC-MD-002
- 23-NREC-MD-003
- 23-NREC-MD-004
- 22-NREC-MD-042-SM1
- 22-NREC-MD-021-SM1
- 22-NREC-MD-030-SM1
- 22-NREC-MD-041-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(s) (17 November 2022 and 15 December 2022) were approved.
- Matters arising from the previous meeting: none.
- Declarations of interest:
  - Chita Murray (23-NREC-MD-004) left the meeting for the review of 23-NREC-MD-004.

Applications

23-NREC-MD-001

- Principal Investigator: Prof. David Keane
- Study title: Adagio Medical Pulsed Field Ablation (PFA) & Pulsed Field CryoAblation (PFCA) for Persistent Atrial Fibrillation (PsAF)
- Lead institution: Blackrock Health, Blackrock Clinic, Rock Road, Blackrock, Co.

  Dublin, A94 E4X7, Ireland
- NREC-MD comments:
  - The NREC-MD noted that the Principal Investigator and/or members of the study team will perform recruitment of participants and engage in the informed consent process. The Committee requests that the role of gatekeeper be introduced into the recruitment and consenting process.
  - The NREC-MD noted that the proposal is a first-in-human study, and that sample size calculation may not be feasible. However, the Committee requests confirmation that the proposed sample size is in line with previous research in this area to provide evidence that the study is sufficiently powered.
  - The NREC-MD noted that the Participant Information Leaflet (PIL) and Informed Consent Form (ICF) have been submitted as one document, and requests that two standalone documents be created.
  - The NREC-MD noted that the documented risks in the PIL currently combine those associated with ablation, and those uniquely associated to the use of the study device(s). The Committee requests that the likelihood of risks be delineated in the PIL such that it is evident which risks are commonly associated with ablation, and which risks are unique to the proposed study device(s). The NREC-MD further requests that all additional risks be included in the PIL which may be uniquely associated with the study device(s); for instance, air embolism and/or thermal injury.

- The NREC-MD noted that the PIL does not sufficiently outline the rationale for the study and the potential benefits to participation. The Committee requests that this information be included, in layperson's terms, such that the participant may assess what the study treatment(s) may offer, when compared to existing, commonly used, approaches.
- The NREC-MD noted that the PIL does not provide sufficient detail regarding the waking state of the participant while experiencing the study treatment(s) and requests that this information be included.
- The NREC-MD requests amendment to, or clarification of, the language in the PIL regarding potential pregnancy.
- The NREC-MD noted that the PIL directs participants to a website for further information. The Committee suggests that the relevant information be summarised into material which may be handed to participants in the event of accessibility difficulties.
- The NREC-MD noted that the ICF does not contain yes/no tick boxes for each consent item. The Committee requests that the ICF be formatted to include same, and additionally requests that consent items which are optional be separated from consent items which are required for study participation.
- The NREC-MD noted that the PIL includes the instruction for the participant to indicate consent to the use of data for future research. The Committee requests that this item (and yes/no tick box) be added to the ICF as an optional item, if applicable.
- The NREC-MD noted the following consent item in the ICF in relation to the participant becoming pregnant during the study (Page 14): 'I know that I cannot get pregnant during the study'. The Committee requests that this item be removed.
- The NREC-MD noted that study data is referred to as 'coded' data, and requests clarification as to whether data will be pseudonymised or anonymised. The Committee considered that the data will be pseudonymised (not anonymised) and highlighted the distinction between the terms under the applicable data protection laws. If, following assessment by the applicant, the terminology is amended by the applicant, such a correction must be reflected in all documentation including, but not limited to, the NREC-MD application form, the data sharing agreement, and the DPIA.
- The NREC-MD requests clarification as to the ability of participants to withdraw consent for data processing following withdrawal of consent to participate in the study.
- The NREC-MD noted that a data retention period of 20 years is proposed. The Committee requests a justification for this duration and requests alignment with the requirements of the Medical Device Regulation (EU) 2017/745 as applicable.
- The NREC-MD requests clarification regarding any potential payment and/or fee schedules; recipient(s), source(s), reimbursement etc.
- The NREC-MD requests clarification regarding any potential conflict(s) of interest.
- The NREC-MD requests a sufficiently detailed copy of the study budget.
- The NREC-MD requests a copy of the applicable organisational insurance policy.

  - The NREC-MD noted that a medical physics expert (MPE) has reviewed and approved the study proposal. The Committee requests confirmation that a radiation protection advisor (RPA) has also completed review and approval of the study proposal.
  - The NREC-MD requests the amendment of administrative errors in the completion of the NREC-MD application form, and alignment between submitted documents with regard to the period of insurance cover.
- NREC-MD decision:
  - *Request for Information*

23-NREC-MD-002

- Principal Investigator: Prof. Gábor Széplaki
- Study title: SECURE - An observational post-marketing study for evaluation of ongoing safety and effectiveness of catheter mapping and ablation using commercially approved BWI medical devices for the treatment of patients with cardiac arrhythmias.
- Lead institution: Mater Private Hospital, 72 Eccles Street, Dublin 7, D07 RD8P, Ireland
- NREC-MD comments:
  - The NREC-MD noted that several specified sub-studies are identified in the protocol which require specified sample sizes. The Committee requests clarification on the analysis process and validity of the study outcomes should the overall 5,000 patients be recruited without reaching the sample sizes required by the sub-studies.
  - The NREC-MD requests that the role of gatekeeper be introduced into the recruitment and consenting process. The Committee requests that all potential study participants are provided with a copy of a Patient Information Leaflet (PIL) and an opportunity to discuss the study with a gatekeeper before their interest in the study is gauged.
  - The NREC-MD requests, when engaging the services of a translator, that a certified translator/translation company is used, to ensure accuracy.
  - The NREC-MD requests that the role of the Study Safety Lead is further outlined in the PIL.
  - The NREC-MD requests that prospective participants are offered 24 hours at minimum to consider their decision to participate in the study, and that this be explicitly documented in the PIL.
  - The NREC-MD requests that the language of the PIL be revised for clarity, with regard to costs and compensation.
  - The NREC-MD requests that the study team or the lead study site provide information to participants regarding their rights, and further requests that the PIL be amended to reflect same.
  - The NREC-MD noted that the Committee will not request access to the personal data of participants, and requests that the PIL be amended to reflect same.

- The NREC-MD requests that certain sections of the PIL be revised for accessibility, to include ‘procedural data collection’ and ‘procedural information’, and that applicable terminology be aligned between the PIL and ICF.
- The NREC-MD noted that the consent form seeks consent for future research, however the information on the types of future research listed in the PIL is broad, implying that blanket consent is being sought. The Committee requests that this is amended. In line with best practice and Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), both participant consent and independent research ethics review should be sought for specific research proposals once they are clearly defined. To that end, in the consent form, the participants should be asked for consent to be contacted in the future for such purposes. Alternatively, future research should be outlined in much greater detail to facilitate a truly informed consent.
- The NREC-MD noted that no specific consent for data anonymisation is being sought, and requests that it is included in the ICF. The Committee further requests, for its own reference, a detailed description of the process of data anonymisation.
- The NREC-MD noted that the study data will be transferred outside of the EU, and requests that a separate consent item be included in the ICF.
- The NREC-MD noted that if a participant withdraws from the study, their data will still be used. The Committee requests that every effort should be made to facilitate withdrawal of participant’s collected data, should they request it.
- The NREC-MD noted that the DPIA from the Mater Private Hospital includes a recommendation from the DPO in the following terms: ‘Ensure robust process in place to check no identifying information sent to sponsor.’ The Committee request a clarification on the measure(s) taken to implement this recommendation.
- The NREC-MD requests clarification on the measure(s) taken to implement certain DPO recommendations, as documented in the DPIA.
- The NREC-MD requests clarification regarding certain aspects of the study budget.
- The NREC-MD requests clarification whether participants will undergo additional, study-specific radiation procedures which are additional to those carried out as a part of standard care.

- NREC-MD decision
  - *Request for Information*

23-NREC-MD-003

- Principal Investigator: Prof. Gábor Széplaki
- Study title: Real world Data collection in subjects treated with the FARAPULSE™ Pulsed Field Ablation system (FARADISE)
- Lead institution: Mater Private Hospital, 72 Eccles Street, Dublin 7, D07 RD8P, Ireland
- NREC-MD comments

- The NREC-MD noted that the application form refers to reporting and dissemination of study findings via http://www.ClinicalTrials.gov and requests clarification whether any other dissemination methods will be used.
- The NREC-MD noted the exclusion criteria and requests a clarification whether these relate specifically to participation in the study or more broadly to participants undergoing the ablation procedure.
- The NREC-MD requests clarification as to which procedures/follow ups are study-specific, and which are standard-of-care. Furthermore, the Committee requests clarification regarding the questionnaires to be utilised.
- The NREC-MD noted that participants will “receive a phone call at 30 days post-procedure to verify adverse events and complications”. The Committee requests clarification why the verification time will be 30 days, and not sooner, following an adverse event/complication.
- The NREC-MD noted that some follow up checks will be conducted by phone and requests clarification whether in person follow up would be more appropriate.
- The NREC-MD noted the proposal to censor the data of participants who withdraw from the study or are deceased prior to 12 months without experiencing a failure event. The Committee queried whether this approach might introduce a bias into the outcomes of the study and requests a justification.
- The NREC-MD requests a justification for the participant follow up time period of 36 months.
- The NREC-MD noted that the study protocol states that potential risks have been listed in the Instructions for Use (IFU). In general, all study related risks should also be included in the protocol. As a result of this proposed approach, the IFU may change over time. The Committee requests confirmation of how changes to the IFU will be dealt with in relation to the clinical investigation, e.g. notification/application for modification.
- The NREC-MD requests that the role of gatekeeper be introduced into the recruitment and consenting process.
- The NREC-MD requests that prospective participants are offered at minimum 24 hours to consider their participation in the study, and that this be explicitly documented in the PIL.
- The NREC-MD requests, when engaging the services of a translator, that a certified translator/translation company is used, to ensure accuracy.
- The NREC-MD requests clarification regarding the involvement of participants of child-bearing potential, and for the management of pregnancy during follow up.
- The NREC-MD requests clarification of the expected attrition rate based on other similar studies, in the context of sample size. Furthermore the Committee requests an assurance that the study findings be valid and provide interpretable outcomes.
- The NREC-MD requests greater clarity and additional detail regarding the means, extent and purpose of data collection, access and sharing.

- Furthermore, the NREC-MD noted that the PIL and ICF document potential future research in broad terms, implying that blanket consent is being sought. The Committee requests that this be amended. In line with best practice and Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), both participant consent and independent research ethics review should be sought for specific research proposals once they are clearly defined. To that end, in the consent form, the participants should be asked for consent to be contacted in the future for such purposes. Alternatively, future research should be outlined in much greater detail, to facilitate a truly informed consent.
- The NREC-MD requests the removal from the PIL of personal contact details for the study team.
- The NREC-MD noted that the PIL includes the following statement which appears to be in conflict with the requirement for study specific insurance policies as set out by the State Claims Agency. The Committee requests clarification as to how participant rights will be protected, should they get injured as a consequence of participating in this study.
    - *"No special arrangements have been made for payment to you for additional treatment resulting solely because of injuries from your participation in this study. No payment will be made by the Study Sponsor or Mater Private Hospital for lost wages, expenses, compensation for pain and suffering, discomfort, or disability"*
- The NREC-MD noted that participants will not be offered reimbursement of study related expenses and requests a justification given the expected commitment of the participants.
- The NREC-MD noted that the itemised study budget includes a fee for serious adverse events and requests clarification on what this fee relates to.
- The NREC-MD noted that the application form does not include a total funding amount for the study and requests that it be provided.
- The NREC-MD requests clarification in the application form in relation to conflict of interest.
- The NREC-MD requests clarification whether participants will undergo additional, study-specific radiation procedures which are additional to those carried out as a part of standard care.

- NREC-MD decision
    - *Request for Information*

23-NREC-MD-004

- Principal Investigator: Dr. Greg Creavin
- Study title: Assessment of post-operative pain after a single-visit root canal treatment using VaryFlex Taper files VFNEO and TruNatomy rotary endodontic files: prospective, open-label trial.

- Lead institution: Beechwood Dental, 9 Dunville Avenue, Ranelagh, D06 EC93, Ireland
- NREC-MD comments
  - The NREC-MD noted that the Principal Investigator declared an economic interest in the study. The Committee were not assured that it did not present a substantial conflict of interest and that it would not compromise the integrity of the clinical investigation.
- NREC-MD Decision
  - Unfavourable

22-NREC-MD-042-SM1

- Principal Investigator: Prof. Robert Byrne
- Study title: A Prospective, Randomized, Non-Inferiority Trial to Determine the Safety and Efficacy of the Biolimus A9™ Drug Coated Balloon for the Treatment of In-Stent Restenosis: First-in-Man Trial (REFORM)
- Lead institution: Mater Private Hospital Eccles St, Inns Quay, Dublin 7, D07 WKW8, Ireland
- NREC-MD decision
  - *Favourable with conditions*
- Associated conditions:
  - The NREC-MD requests that the study insurance policy is extended in line with the extended duration of the study.

22-NREC-MD-021-SM1

- Principal Investigator: Prof. Robert Byrne
- Study title: LiquID Guide Catheter Extension Safety Study
- Lead institution: Mater Private Hospital, Eccles St, Dublin 7, D07 WKW8, Ireland
- NREC-MD decision
  - *Favourable with conditions*
- Conditions
  - The NREC-MD requests that a confirmation of appropriate financial and indemnity arrangements for the additional site is provided to the National Office.

22-NREC-MD-030-SM1

- Principal Investigator: Dr Umer Salati

- Study title: A randomized trial of ultrasound-facilitated, catheter-directed, thrombolysis versus anticoagulation for acute intermediate-high risk pulmonary embolism: The higher-risk pulmonary embolism thrombolysis study
- Lead institution: Mater Misericordiae University Hospital, Eccles St, Dublin 7, Ireland
- NREC-MD decision
  - *Favourable*

22-NREC-MD-041-SM2

- 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
- Lead institution: St Vincent's University Hospital, Elm Park, Dublin 4, D04 T6F4, Ireland
- NREC-MD decision
  - *Favourable*

- AOB:
- The Chairperson thanked the Committee and closed the meeting.