NATIONAL OFFICE FOR RESEARCH ETHICS COMMITTEES

National Research Ethics Committee

NREC-MD Meeting Minutes

15th February 2024

Attendance

Name	Role
Prof. Barry O'Sullivan	Chair, NREC-MD
Prof. Mary Sharp	Deputy Chair, NREC-MD
Prof. Declan Patton	Deputy Chair, NREC-MD
Dr Daniel Coakley	Member, NREC-MD
Dr Mireille Crampe	Member, NREC-MD
Dr Ruth Davis	Member, NREC-MD
Dr James Gilroy	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
Prof. Tom Melvin	Member, NREC-MD
Prof. Cara Martin	Member, NREC-MD
Prof. Therese Murphy	Member, NREC-MD
Dr Declan O'Callaghan	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
Prof. Anne Parle McDermott	Member, NREC-MD
Ms Riona Tumelty	Member, NREC-MD
Prof. Mahendra Varma	Member, NREC-MD
Ms Simone Walsh	Member, NREC-MD
Ms Chita Murray*	Programme Manager, National Office for Research Ethics Committees
Dr Louise Houston	Project Officer, National Office for Research Ethics Committees

*Drafted minutes. Dr Lucia Prihodova (Programme Manager, National Office for Research Ethics Committees) contributed to drafting of the minutes.

Apologies: Dr Caitriona Cahir, Dr Owen Doody, Dr Sarah McLoughlin, Prof. Susan O'Connell, Mr Peter Woulfe

Quorum for decisions: Yes

Agenda

- Welcome (Chairperson)
- Report on Committee business
- Minutes of previous meeting
- Declarations of interest
- 23-NREC-MD-038-R1
- 23-NREC-MD-018-SM1-R1
- 23-NREC-MD-039-R1
- 23-NREC-MD-040
- 24-NREC-MD-001
- 24-NREC-MD-002
- 24-NREC-MD-003
- 24-NREC-MD-004
- 23-NREC-MD-006-SM1
- 22-NREC-MD-017-SM1
- 23-NREC-MD-024-SM1

- 23-NREC-MD-012-SM1
- 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) (18th January 2024) were approved.
- Matters arising from the previous meeting: none
- Declarations of interest:
  - Prof. Jim O'Neill (23-NREC-MD-018-SM1) did not read the documentation associated with application 23-NREC-MD-018-SM1 and vacated the meeting while the study was under discussion.
  - Prof. Jim O'Neill (24-NREC-MD-004) did not read the documentation associated with application 24-NREC-MD-004 and vacated the meeting while the study was under discussion.
  - Dr Paul O'Connor (23-NREC-MD-018-SM1) did not read the documentation associated with application 23-NREC-MD-018-SM1 and did not participate when the application was under discussion.
  - Ms Ríona Tumelty (23-NREC-MD-006-SM1) did not read the documentation associated with application 23-NREC-MD-006-SM1and did not participate when the application was under discussion.
  - Dr Declan O'Callaghan (23-NREC-MD-006-SM1) did not read the documentation associated with application 23-NREC-MD-006-SM1 and did not participate when the application was under discussion.

Applications

23-NREC-MD-038-R1

- Principal Investigator: Prof. Niamh Nowlan
- Study title: Fetal Movement Device Clinical Investigation: Demonstrating the safety and performance of a novel wearable fetal movement monitor
- Lead institution: University College Dublin, School of Mechanical and Materials Engineering, Belfield, Dublin 4, D04 V1W8.
- NREC-MD Decision
  - *Favourable with conditions*
- Associated conditions

- An expert in clinical psychology is given the opportunity to comment on the aspects of the study related to the device which have the potential to induce anxiety in participants.
- Informed Consent Form to be updated to align with the Participant Information Leaflet which discusses the use of fully anonymised data for future research.

23-NREC-MD-018-SM1-R1

- Principal Investigator: Dr Ken McDonald
- Study title: First in Human Clinical Investigation of the FIRE1™ System in Heart Failure in Patients
- Lead institution: St. Vincent's University Hospital, Elm Park, Dublin 4, D04 T6F4.
- NREC-MD Decision
  - *Request for further information*
- Further information requested
  - The language in the Participant Information Leaflet / Informed Consent Form is amended to is amended to remove language which could be perceived as communicating a benefit.
  - Participant-facing information is amended to ensure participants are fully informed, in an accessible manner (terminology and diagrams), with regard to the potential implications of participation in the study in relation to the outcomes of previous studies which included the Gen1 iteration of the device.
  - Specifically, participants must be informed that, of the four (4) Gen1 devices which have been implanted, each has fractured, and some have lost signal, and about the long-term implications of same.
  - Furthermore participants must be informed about the potential for the Gen2 device to exhibit fractures and any additional and/or associated risks of implantation with the Gen2 device.

23-NREC-MD-039-R1

- Principal Investigator: Dr Janusz Krawczyk
- Study title: Collection and Processing of Peripheral Blood (PB) and Bone Marrow (BM) Specimens from healthy volunteers for Analytical Performance Evaluation of the BD Cytognos™ MM-MRD Reagent Panel on the BD Flow Cytometer Systems
- Lead institution: HRB Clinical Research Facility, University Hospital Galway, Newcastle Rd, Galway, H91 YR71.
- NREC-MD comments
  - The NREC-MD noted difficulty in deciphering the sequence of procedural steps within the overall study design.

- The NREC-MD noted that blood samples of prospective participants (healthy volunteers) will be screened for the presence of HIV, Hepatitis B and C and was not satisfied that protection of laboratory analysts is sufficient justification to place burden on the participant in the form of this proposed virus screening procedural step.
- The NREC-MD noted a discrepancy between clinical research form and contract negotiations suggest in relation to tests to determine presence or absence of haematological abnormalities.
- Furthermore the Committee noted that in the context of this application the presence of haematological abnormalities detected during the eligibility screening of healthy volunteers, ought to be referred for further assessment via the appropriate clinical care pathways, even if the volunteer does not participate in the study, and that such accidental findings be disclosed to the participant.
- The NREC-MD noted uncertainty regarding contractual arrangements which currently under review and have not yet been established, role of the various protagonists, and the exact activities which will be carried out in the accredited laboratory, the hospital, the clinical research facility and the BD Research Centre Ireland testing facility (Limerick).
- With regard to contractual arrangements, the Committee noted lack of clarity whether all parties have agreed to the contents of an established agreement, and whether contracts will be in place between the Sponsor and laboratories which are suitably accredited for the activities which they will undertake.
- The NREC-MD acknowledged that the BD Research Centre Ireland testing facility is not accredited to provide diagnosis for human treatment. However, the Committee identified a lack of clarity in the application with regard to whether the alternative laboratory listed in the application (Haematology Testing Laboratory, University of Galway, University Road, Galway) has/will have the appropriate accreditations in place to process and test biological samples of human origin, and to interpret results. Data gathered during testing of the blood/bone marrow samples must be fit-for-purpose, aligning with the intended aims of the study i.e. data must be eligible for submission to obtain a CE mark. The extraction of bone marrow samples from healthy volunteers would be unethical if the resulting test data cannot be used.
- The NREC-MD noted a lack of clarity with regard to the identity (e.g. role(s)) of the individual/team who will decide on the ‘eligibility’ of prospective participants to be enrolled in the study.

- NREC-MD Decision
  - *Unfavourable*

23-NREC-MD-040

- Principal Investigator: Prof. Conleth Murphy
- Study title: Clinical Performance Study for the use of FOLR1 (2.1) IHC Clinical Trial Assay in IMGN853-0420, a Multicenter, open-label, phase 2 study of carboplatin plus

mirvetuximab soravtansine followed by mirvetuximab soravtansine continuation in folate receptor-alpha positive, recurrent platinum-sensitive, high-grade epithelial ovarian, primary peritoneal, or fallopian tube cancers following 1 prior line of platinum-based chemotherapy

- Lead institution: Bon Secours Hospital, College Road, Cork, T12DV56.
- NREC-MD Decision
  - *Request for further information*
- Further information requested
  - The NREC-MD noted that the Pre-screening Participant Information Leaflet/Informed Consent Form (PIL/ICF) requires additional information / amendments.
  - Confirmation that all study costs associated with participation in the clinical trial and performance study will be paid by the Sponsor.
  - The NREC-MD noted a lack of clarity with regard to the location of testing and storage of samples, and the duration of storage until destruction. The Committee requests that this information be more clearly outlined for prospective participants.
  - Separate consent is sought for transfer of data to countries outside the EU.
  - The NREC-MD requests clarification on the circumstances under which suitable prospective participants may/may not be contacted and invited to attend pre-screening.
  - The NREC-MD requests clarification on steps which will be taken is over the course of the study results become available that are unexpectedly relevant to the patient's treatment.
  - The NREC-MD requests confirmation that the applicable valid insurance policies will be in place for the duration of the study.
  - The NREC-MD noted that the protocol indicates that either archival tumour samples may be used for testing with the investigational in vitro diagnostic device, or an additional biopsy may be conducted to collect a fresh sample. The Committee requests clarification in the response letter or NREC-MD application form as to the need for collection of the fresh sample, and confirmation that the Sponsor will bear all such costs associated with the study.

24-NREC-MD-001

- Principal Investigator: Prof. Marcus Kennedy
- Study title: Use of electromagnetic tracking to monitor patient breathing movement during bronchoscopy to assess registration errors with respect to pre-operative CT images
- Lead institution: Cork University Hospital, Wilton Road, Cork, T12 YK23.
- NREC-MD Decision
  - *Favourable with conditions*

- Associated conditions
  - The NREC-MD requests a confirmation that the use of radiopaque markers during CT diagnostic imaging will not interfere with the accurate interpretation of these scans.
  - The NREC-MD requests a clarification on steps taken to mitigate risks relating to electrical safety.
  - The NREC-MD requests that the participant's GP be informed about their involvement with this study. A copy of the GP letter template should be provided to the National Office for Research Ethics Committees (National Office).
  - The NREC-MD requests confirmation that the informed consent process will be completed by the PI or by an authorised designee of the PI (as per Section 5.8.2 of ISO 14155:2020) who is a member of the investigating team who is appropriately qualified under national law (as per Article 63(2)(c) of the Medical Device Regulation (EU) 2017/745).
  - The NREC-MD requests a clarification on how the pseudonymised data from CT scans will be transferred from Mallow General Hospital to the Tyndall institute.
  - The NREC-MD requests that section O28 of the application form is signed by an expert in medical physics and updated form is provided to the National Office.
  - The NREC-MD application form (G5) indicates that a convenient time will be arranged for participants to meet a research staff member. This implies that participants will need to attend the hospital for an extra visit. The Committee requests this is clearly stated in the PIL/ICF.
  - The NREC-MD requests that potential benefits stated in participant facing documents is updated to highlight that that the data generated has the potential to help develop algorithms which could potentially improve the accuracy and precision needed by doctors to target diseases like lung cancer and other airway diseases.
  - The NREC-MD requests that participant facing documents are updated to clearly outline the timing of study procedures.

24-NREC-MD-002

- Principal Investigator: Dr Karen Cadoo
- Study title: Diagnostic Protocol for VENTANA FOLR1 (FOLR1-2.1) CDx Assay for ImmunoGen Study IMGN853-0421
- Lead institution: St. James's Hospital, Dublin 8, D08 NHY1.
- NREC-MD Decision
  - *Request for further information*
- Further information requested
  - The NREC-MD noted that the Application Form, Pre-screening Participant Information Leaflet/Informed Consent Form requires additional information / amendments for accessibility and clarity.

- The NREC-MD requests a clarification on who will have access to participant's p*ersonal Information and for what purpose.*
- The NREC-MD requests a clarification with regard to the third-party testing facilities which samples may be transferred to, etc.
- The NREC-MD requests that reasonable participant expenses be reimbursed.
- The NREC-MD requests that the section entitled 'Optional Consent for Conduct of Secondary Research' highlights that consent for future use of tumour samples and/or other forms of data is optional to comply to ensure compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018.
- The NREC-MD requests a please amend the language to reflect that has been reviewed by the National Research Ethics Committee(s) rather than the National Office.
- The diagnostic protocol indicates that 'all local, regional and institutional policies must be followed by all parties involved' as requirements can vary by jurisdiction. The Committee requests a confirmation that the associated requirements of the EU and the Rep. of Ireland will apply.
- The NREC-MD requests additional information on the activities associated with the performance study, the associated scientific justification and the termination criteria which apply to the performance study/IVD.
- The NREC-MD requests that section H of the application form on inclusion of participants who lack decision-making capacity is completed.
- In relation so section K4 (b) of the application form, the Committee requests a summary response at a minimum in place of exclusively referencing separate documentation. Please make reference to the protection of data which is generated during the performance study in the specific context of the Rep. of Ireland.
- The NREC-MD requests further clarification to the application form with regard to the justification for a fresh biopsy to be taken, and repeat testing to be conducted, along with a clarification on how the test result from the archival sample will be managed/processed in this scenario.
- The NREC-MD requests clarification on section M1 of the Application Form: The NREC-MD noted that the applicant has indicated that the study will involve the generation of genetic data, that participants will be informed of clinically relevant important incidental findings. This information does not align with the information provided in the pre-screening PIL/ICF. Please reassess whether genetic data will be generated, and resubmit amended documents as applicable.
- The NREC-MD noted that the DPIA makes reference to BRCA1 genetic testing. The Committee seeks clarification as this is not referred to elsewhere in the submitted documents e.g. PIL/ICF, NREC-MD application form.
- The NREC-MD noted that neither a total budget figure nor financial information for the performance study was included in the submitted documents, and requests that such information be provided as applicable.

24-NREC-MD-003

- Principal Investigator: Prof. Briain MacNeill
- Study title: A Post-Market Registry of the BioFreedomTM Ultra CoCr Biolimus A9TM coated coronary stent system
- Lead institution: Dept. of Cardiology, Galway University Hospital, Newcastle Rd, Galway, H91 YR71.
- NREC-MD Decision
  - *Request for further information*
- Further information requested
  - The NREC-MD noted that the application form requires an overall review due to number of typographical errors and inconsistencies within submitted details and requests that these be updated, ie references to NHS and/or UK hospitals.
  - The NREC-MD requests a clarification on the recruitment and consenting process, and on any procedures which will be in place to minimise any bias posed by the recruitment process.
  - The NREC-MD requests a confirmation that participants will be given a minimum of 24 hours to consider their participation in the study.
  - 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 Committee noted that data will be transferred to countries which are outside of the EU, and with whom an EU adequacy decision is not in place and requests evidence of data transfer agreements.
  - The NREC-MD seeks clarification of the process of source data verification and purpose of adjudication of the data.
  - The NREC-MD noted that images that are collected will be encrypted. As imaging is not mentioned elsewhere in the application, the Committee requests clarification.
  - The NREC-MD requests that all data breaches will be reported to the Irish Data Protection Commission.
  - The NREC-MD requests additional information with regard to the practice of remote data monitoring, and the procedures which will be in place to facilitate this.
  - The NREC-MD requests Section O of the application form is completed, including signature by a Medical Physics Expert, or provide a justification as to why this section is not applicable.

- As the device is a drug-eluting device containing Biolimus A9 the NREC-MD requests Section P of the Application Form is completed, or a justification as to why this section is not applicable is provided.
- The NREC-MD noted that the Participant Information Leaflet and Informed Consent Form (PIL/ICF) requires additional information/amendments due to typos and overly technical language not suitable for a layperson, or oversights ie sections referring to the corresponding lead Principal Investigator in Ireland, Prof. Briain MacNeill.
- The NREC-MD noted that Prof MacNeill has been recorded as the Sub-Investigator on the submitted CV. The Committee requests that this role be updated to Principal Investigator.
- The NREC-MD noted that a Clinical Trial Indemnity Form (CTIF) for St James's Hospital has not been provided.
- The NREC-MD noted that applicable insurance cover does not appear to be in place in the event of a registry data breach and requests a clarification on the arrangements which will be in place in order to provide compensation to participants, as applicable, in the event of a data breach.
- The NREC-MD requests a detailed study budget which includes reference to this funding, a clarification if a start-up payment be provided to study sites and whether the Principal Investigator (PI) will be provided with any additional fees/ payments. If the PI will be provided with additional payments, please provide a copy of the financial disclosure form.

24-NREC-MD-004

- Principal Investigator: Dr Darren Mylotte
- Study title: InvEstigation of the safety and performance of the NVT ALLEGRA Plus THV SysteM in Patients with severe aortIc stenosis or failed suRgical aortic bioprosthEsis (EMPIRE II)
- Lead institution: University Hospital Galway, Newcastle Rd, Galway, H91 YR71.
- NREC-MD Decision
  - *Request for further information*
- Further information requested
  - The NREC-MD noted that a number of documents require additional information/amendments for clarity and accessibility.
  - The NREC-MD requests clarification on who will approach the prospective participant to determine their interest in participating in the study. The Committee suggests that this activity be assigned to an authorised designee of the Principal Investigator (as per ISO 14155:2020), who is a member of the investigating team appropriately qualified under national law (as per Article 63 of the Medical Device Regulation (EU) 2017/745).

- The NREC-MD requests clarification on decision making capacity and potential inclusion in the study.
- The NREC-MD requests clarification on whether prospective participants may be allowed the advised 24 hours to consider their participation, and present a justification if not.
- The NREC-MD requests that reasonable efforts are made to allow access to the study for participants for whom English is not their native language, or who do not speak English. 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 the translation certificates submitted to the NREC-MD as a non-substantial modification in advance of the distribution of translated documents.
- The NREC-MD requests clarification on whether any of the radiation procedures will be carried out on the Mater site.
- The NREC-MD noted that two separate PIL/ICFs templates have been used i.e. one for each site. The Committee requests that one PIL/ICF document be submitted in order to standardise, and avoid discrepancies in, the information which is provided to participants. Applicable details (logo, contact details etc.) are then updated as applicable for each site.
- With regard to the alternative methods of treatment which are outlined in the PIL/ICF, the Committee requests rationale for not including Cardiac Surgery as a specific alternative.
- The NREC-MD noted (e.g. NREC-MD application form, E1) that the study device is an updated version of an existing device, designed with the intention of improving both the immediate and long-term results of valve implantation. The Committee suggests that this be documented in the PIL/ICF as a point of relevant information to prospective participants.
- The NREC-MD requests a confirmation that safety reporting pathways will be followed as applicable under the EU regulations and legislation of the Rep. of Ireland.
- With regard to the potential for disclosure of encrypted personal data, the Committee requests clarification for the participant that their encrypted personal data would typically be disclosed to a National Research Ethics Committee only in the context of a safety report.
- The NREC-MD requests clarification on who will have access to partcipant personal data.
- With regard to data processing information in the PIL/ICF, the NREC-MD requests clarification how collected data will be managed in the event of participant withdrawal and that a an explicit line item in the ICF which seeks consent for the transfer of data to third parties as applicable is included.

23-NREC-MD-006-SM1

- Principal Investigator: Dr. Adrian Murphy

- Study title: An Open-label Randomized Phase 3 Study of Tucatinib in Combination with Trastuzumab and mFOLFOX6 versus mFOLFOX6 given with orwithout either Cetuximab or Bevacizumab as First-line Treatment for Subjects with HER2+ Metastatic Colorectal Cancer
- Lead institution: Beaumont Road, Dublin 9, D09V2N0.
- NREC-MD Decision
  - *Request for further information*
- Further information requested
  - The NREC-MD noted that the applicant has submitted for review redlined versions 3, 4 and 5 of the immunohistochemistry investigator's brochure (IHC IB), with version 5 showing only the tracked changes/redlines from version 4 to 5. The Committee requests that the changes from versions 2 through 5 be made visible, clarified and/or otherwise outlined in a more readily accessible format.
  - The NREC-MD requests clarification on whether any/all of those changes were categorised as non-substantial modifications which do not typically require review by Committee, and are submitted to the National Office as notifications.
  - The NREC-MD noted that the substantial modification application form (B.14) indicates that the proposed changes include a “modification that affects the safety/physical/mental integrity of participants or to the risk/benefit assessment for the study”. The Committee was unable to determine within the submitted documents what aspects of the changes to the performance study (PS) components of this combined trial will impact on the above considerations, or whether the PS documents as now presented more accurately reflect the risk/benefit assessment which is actually unchanged. The Committee requests clarity on how the substantial modification impacts on the integrity of participants or the risk/benefit assessment.
  - The NREC-MD noted the addition of the following statement to the below-listed document: “retesting might slightly delay the acquisition of an evaluable result but will have no other effect on the patient”. The Committee commented that retesting will delay the decision to include the participant in the trial (or not) and will potentially delay the start of the treatment, even if only slightly and that the wording should be amended

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22-NREC-MD-017-SM1

- Principal Investigator: Prof. Rustom Manecksha
- Study title: Real world evidence observational study to evaluate performance and safety of intravesical sodium hyaluronate (Cystistat®) in the treatment of patients with interstitial cystitis (IC)/bladder pain syndrome (BPS)
- Lead institution: Department of Urology, Tallaght University Hospital, Tallaght, Dublin, D24 NR0A.
- NREC-MD Decision
  - *Favourable*

23-NREC-MD-024-SM1

- Principal Investigator: Dr Gabor Szeplaki
- Study title: Luma Vision's feasibility study on the VERAFEYE system (LUMINIzE)
- Lead institution: Mater Private Hospital (Dublin), Heart & Vascular Centre, 72 Eccles Street, Dublin 7, D07 RD8P.
- NREC-MD Decision
  - *Request for further information*
- Further information requested
  - The NREC-MD noted that imaging data will no longer be collected via insertion to the left atrium. The Committee requests clarification on why this change is proposed, and whether the change is based on safety data collected for this study to-date.
  - The NREC-MD requests clarification on whether the Section "Ability to visualize the LA from the RA" refers to the ability to visualize the LA using the VERAFEYE imaging catheter, or other imaging tools.

23-NREC-MD-012-SM1

- Principal Investigator: Dr Maeve Lowery
- Study title: Diagnostic Protocol for VENTANA FGFR2b (FPR2-D) Assay for Amgen Study 20210096 (CTIMP: A Randomized, Multi-Center, Double-blind, Placebo-controlled Phase 3 Study of Bemarituzumab plus Chemotherapy versus Placebo plus Chemotherapy in Subjects with Previously Untreated Advanced Gastric or Gastroesophageal Junction Cancer with FGFR2b Overexpression)
- Lead institution: Mater Private Hospital, Heart And Vascular Centre, 72 Eccles Street, Dublin 7, D07 RD8P.
- NREC-MD Decision
  - *Favourable*

- AOB:
- Programme Manager updated the Committee with regard to the below legislative change in the Rep. of Ireland:
  - Revoked: S.I. No. 260/2021 - European Union (National Research Ethics Committee for Clinical Investigations of Medical Devices) Regulations 2021
  - Replaced with: S.I. No. 671/2023 - European Union (National Research Ethics Committees for Clinical Investigations of Medical Devices) Regulations 2023

- The Committee thanked Ms Chita Murray for the great support she gave to the Committee in her role as the interim Programme Manager over the last year.
- The Chairperson thanked the Committee and closed the meeting.