NATIONAL OFFICE FOR RESEARCH ETHICS COMMITTEES

National Research Ethics Committee

NREC-MD Meeting Minutes

18th January 2024

Attendance

Name	Role
Prof. Barry O'Sullivan	Chair, NREC-MD
Prof. Declan Patton	Deputy Chair, NREC-MD
Dr Caitriona Cahir	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 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 Paul O'Connor	Member, NREC-MD
Mr Damien Owens	Member, NREC-MD
Prof. Anne Parle McDermott	Member, NREC-MD
Ms Riona Tumelty	Member, NREC-MD
Mr Peter Woulfe	Member, NREC-MD

Name	Role
Dr James Gilroy	Member, NREC-MD
Dr Daniel Coakley	Member, NREC-MD
Prof. Cara Martin	Member, NREC-MD
Prof. Jim O'Neill	Member, NREC-MD
Ms Simone Walsh	Member, NREC-MD
Chita Murray*	Programme Manager, National Office for Research Ethics Committees
Louise Houston	Project Officer, National Office for Research Ethics Committees
Dr Emily Vereker	Head, National Office for Research Ethics Committees

*Drafted minutes

Apologies: Prof. Mary Sharp (Deputy Chair), Dr Frank Houghton, Prof. Therese Murphy, Dr Clare O'Connor, Prof. Mahendra Varma, Mr Peter Woulfe

Quorum for decisions: Yes

Agenda

- Welcome (Chairperson)
- Report on Committee business
- Minutes of previous meeting
- Declarations of interest
- 23-NREC-MD-035
- 23-NREC-MD-036
- 23-NREC-MD-037
- 23-NREC-MD-038
- 23-NREC-MD-039
- 23-NREC-MD-015-SM1
- 22-NREC-MD-036-SM3
- 23-NREC-MD-010-SM2
- 23-NREC-MD-018-SM1
- 22-NREC-MD-039-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) (16th November 2023, 21st December 2023) 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.
  - 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.

Applications

23-NREC-MD-035

- Principal Investigator: Dr Lisa Costelloe
- Study title: Evaluation of Novel Digital Biomarkers in a Diverse Multiple Sclerosis Cohort
- Lead institution: Beaumont Hospital, Beaumont Road, Beaumont, Dublin 9, Ireland
- NREC-MD Decision
  - *Request for further information*
- Further information requested

Participant Information Leaflets (PILs):

The NREC-MD noted that these documents require additional information/amendments. The Committee requests that a revised copy be submitted, with updates at applicable sections:

- Please update the cover page of both the PIL to be distributed to patients with Multiple Sclerosis, and the PIL to be distributed to healthy control group to include reference to the alternative PIL, so as to avoid confusion among participants.
- Page 2: With regard to the below phrase, which appears in both the PIL to be distributed to patients and the PIL to be distributed to the healthy control group, please reword as indicated:
  - 'we need to know if these medications are effective for [individual] patients so that they can get the best care possible'
- Page 3: Please confirm the number of site and/or home visits including follow-up visits which will be included in the schedule of visits for the healthy control group, as differences have been observed in the submitted documents e.g. every three months (PIL), every six months (protocol).

- Page 4: With regard to the below phrasing, which appears in both the PIL for patients and for PIL for the healthy control group, please use standardised, more specific terminology which communicates in more practical terms the assessment of risk i.e. suitable for a lay person. Please also outline for the participant(s) the likelihood of such events being temporary or permanent.
  - "There is a very low residual risk that the device could potentially injure your eye or face in case of malfunction or incorrect use"
  - "There is a remote risk of a laser-induced blind spot adverse event occurring"
- Page 5 (PIL for healthy control group): With regard to the below statement in this document, please clarify in an appropriate section of the document (and throughout the submitted documents as applicable), that there is a potential for the discovery of abnormal findings, and what the implications might be for the participant.
  - "It also allows for results to be traced back to a participant should any abnormalities be identified"
- Page 7: With regard to the future use of data as outlined in the PIL, please ensure that the PIL and informed consent form (ICF) are in compliance with data protection regulations and legislation, including the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), 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.

Recruitment:

- Clinical Investigation Plan (Section 5.3): notes that 'sedation in the past 24 hours' is a contraindication to testing with the device. Should patients who are prescribed sedative medications be excluded from the study? This may be somewhat covered by exclusion criteria 1 ('undergoing medical treatment judged not to be medically compatible') but could be clearer.
- NREC-MD Application Form (F5): Please provide further information and clarity with regard to the recruitment/consenting plan for healthy volunteers, in the application form and in any other relevant documentation (e.g. Clinical Investigation Plan (Section 4.1)).
- NREC-MD Application Form (F6): With regard to the below statement, please provide NREC-MD with drafts of the social media adverts which will be used for the recruitment of participants, in line with the requirement to submit participant-facing material to the Committee.
  - "Healthy volunteers will be sought via the use of posters and social media adverts within the Beaumont Hospital and RCSI community".
- NREC-MD Application Form (F11, J3): Please confirm whether pregnant participants will be included in the study and align discrepancies in the submitted documents as applicable.
- NREC-MD Application Form (F11): indicates that participants will include adults in emergency situations. Please confirm if this is correct, update the submitted documents in line with this proposal, and apply to NREC-MD accordingly.

- NREC-MD Application Form (G3): with regard to the proposed recruitment steps, the NREC-MD suggests that potential participants be given a minimum of 24 hours to consider their participation following discussion with the clinical research nurse.
- Advertisement Poster: Please amend the name of the Committee from “the National Regulatory Ethics Committee in Ireland” to “the National Research Ethics Committee for Medical Devices”.

Insurance & Financial Arrangements

- The NREC-MD noted that the insurance documents submitted for this study are quotations only. The committee seeks assurance that insurance policies will be in place and renewed as appropriate to cover the duration of the study.
- With regard to the amount allocated in the budget for study personnel, please confirm the figure(s) provided, and provide an indication of payment(s) to the Principal Investigator.

23-NREC-MD-036

- Principal Investigator: Prof. Faisal Sharif
- Study title: Distal Evaluation of Functional performance with Intravascular sensors to assess the Narrowing Effect: Guided Physiologic Stenting (DEFINE GPS)
- Lead institution: University Hospital Galway, Newcastle Rd, Galway, H91 YR71
- NREC-MD Decision
  - *Request for further information*
- Further information requested

NREC-MD Application Form:

The NREC-MD noted that the document requires additional information/amendments. The Committee requests that a revised copy be submitted, with updates at applicable sections:

- E4: Please comment on whether the collection of healthcare resource data will be limited to sites in the United States.
- F13: Please note that the information in this section is incomplete i.e. the final sentence on the explanation of procedures in the physiology-guided arm of the study has been truncated.
- F16: In the below statement, please amend to ‘inherent risk’ to better illustrate the risk profile associated with the device to be used in this study.
  - “Use of any interventional device in the coronary arteries has an incidental risk that comes with it”.
- G6: The NREC-MD application form advises that a minimum of twenty-four (24) hours be given to prospective participants to consider their participation in a study, and the applicant’s response includes the following statement; “due to the nature of this research potential limited reflection time is accepted”.

  - The Committee acknowledge that the intervention is not anticipated to be emergent, and seek clarification as to why the advised twenty-four (24) hours cannot be made available.
  - In addition, please give an indication of the minimum anticipated amount of time that participants may be given to read and understand the applicable participant-facing documents (PIL/PIS and ICF).
  - Alternatively, if the intervention is likely to be emergent for some participants, the applicant should consider whether consent under Article 68 (MDR) is applicable i.e. 'clinical investigations in emergency situations' and amend their application to NREC-MD accordingly.

- G8: With regard to the inclusion of participants who do not speak English, please be advised that the NREC-MD does not consider that the presence of an interpreter alone is sufficient to safeguard the rights of the participant, and requests that appropriately translated copies of participant-facing documents be provided to participants. Translation certificates for the use of translated documents should be submitted to the NREC-MD as a non-substantial modification in advance of distributing translated documents.
- K19: The NREC-MD application form states that data will be archived by the Sponsor for a period of fifteen (15) years. The PIL/PIS (Section 11.9) states the data will be retained for at least twenty-five (25) years. Please clarify.

Participant Information Leaflet/Sheet (PIL/PIS):

The NREC-MD noted that the document requires additional information/amendments. The Committee requests that a revised copy be submitted, with updates at applicable sections:

- The submitted budget notes that remuneration of expenses will be made available to participants, however this is not documented in the PIL/PIS. Please outline for the participant that such remuneration will be available.
- (2nd para.): Please consider whether the language in this section is misleading, as the operator may decide to use fractional flow reserve (FFR) at the time of performing the procedure.
- 1.0: Please consider whether use of the wording 'new approach' in the below statement could influence the participant with regard to their perception of the treatment options, and whether a more suitable term is appropriate, such as 'other approach'.
  - "You have a 50%-50% chance as to whether you will receive the routine approach ("angiographic guidance") or the new approach ("guided physiologic stenting" - GPS) to guide your study treatment".
- 2.0: Please include a brief explanation of the meaning of term 'Sponsor' in the context of the study, as the term may be unfamiliar to participants.
- 3.0: With regard to the below statement, please outline for the NREC-MD and in the PIL/PIS how participants will be involved in the two year follow-up period.

  - "Overall, your participation in the study will last about 2 years and follow-up period will extend over another two years, so the overall study duration is expected to be four years before the results are known".

- 3.0: Please confirm how many participants will be recruited in the Republic of Ireland and align this figure throughout the applicable documents e.g. the PIL/PIS, the NREC-MD application form, and the submitted budget.
- 4.0: With regard to the below statement, please note that documented consent of the identified contact person will be required.
  - "A person identified by you may be reached by the study doctor regarding how to reach you".
- 4.0: The applicant proposes to access the Civil Register to ascertain participant's whereabouts in the event that a participant appears lost-to-follow-up. Please confirm whether this proposed practice has been given careful consideration by the study team/Sponsor, and whether such an activity is an appropriate use of this public resource. Please note that the explicit consent of the participant is required for the use of their personal data in accessing information from the Civil Register.
- 11.3: With regard to the below statement, please clarify the type of data (anonymised/pseudonymised) to be sold and whether participants will be given the opportunity to consent to the sale of their data.
  - "If your encoded study data are sold, you will not benefit from this".

Informed Consent Form (ICF):

The NREC-MD noted that the document requires additional information/amendments. The Committee requests that a revised copy be submitted, with updates at applicable sections:

- The PIL/PIS (Section 11.3) 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.
- The NREC-MD application form (Section E6) states, if participants would like to be kept informed with regard to the results of the study, that they will be provided with the general results. The Committee requests that this be enabled by providing a tick box in the informed consent form which is optional and separate ('unbundled') from the main consent items, such that participants may decline consent for this item, yet still participate in the study.
- Please include an additional consent line item to seek consent for the transfer of data outside of the EU.

Insurance

- The NREC-MD requests confirmation from the Sponsor that the period of product liability cover will be extended as required to cover the duration of the study.

Contracts:

- The NREC-MD noted that the submitted Clinical Investigation Agreement is intended for use by named entities which are located in a jurisdiction outside of the Republic of Ireland. The Committee requests that an applicable copy of the agreement be submitted.

HSE Privacy Impact Assessment Form

- The NREC-MD noted that a number of text boxes contain incomplete information e.g. pages 4, 5, 7, 8, 10, 11 etc. The Committee requests that a copy of the completed HSE privacy impact assessment form be submitted in which all information is visible.

23-NREC-MD-037

- Principal Investigator: Prof. Seamus O'Reilly
- Study title: Clinical Performance Study Plan for Ki-67 IHC MIB-1 pharmDx (Dako Omnis) on early breast cancer specimens used to identify subjects for enrolment in AstraZeneca's Phase III CAMBRIA-2 trial (D8535C00001-IVD)
- Lead institution: Cork University Hospital, Wilton, Cork, Ireland
- NREC-MD Decision
  - *Request for further information*
- Further information requested

Clinical Performance Study Plan:

- The NREC-MD requests additional information in relation to identification, transport and handling of clinical samples/specimens to be used for testing in the performance study. The Committee seeks assurance, with regard to tissue blocks being transferred off-site to a central diagnostic testing laboratory, that applicable control/security and contractual measures will be in place. Please clarify:
  - How long will blocks be retained at the receiving laboratory?
  - What measures will be in place to ensure that blocks are stored securely?
  - With regard to the anonymisation/pseudonymisation of samples, will patient (as distinct from participant) identifiers remain on the blocks once they leave the study site and, if so, will they be obscured?
  - Has consideration been given to cutting samples from the block at the source laboratory, at which point pseudonymisation would be straightforward?
  - Will cases be returned to the study site, and will appropriate procedures, contracts and material transfer agreements be in place for bidirectional transfers?

  - What criteria will be used to select blocks for transfer from the study site, and who will be responsible for selecting the blocks e.g. local pathologists?
  - How will unused excess samples at the receiving laboratory be managed, destroyed etc.?
  - Please comment on whether the destruction of unused excess samples could compromise ongoing participant medical care.
- The NREC-MD noted that additional detail with regard to immunohistochemical evaluation and scoring etc. is provided in the Agilent scoring guideline (document 19b) including appendix (document 19c) which is submitted in addition to the clinical performance study plan (document 14). The Committee requests additional detail which does not appear to be included within these submitted documents, to illustrate how the risks of false positive/negative results, associated with the diagnostic, are being mitigated:
  - Is the performance evaluation protocol a consensus panel review and, if so, by how many reviewers?
  - Is an adjudication panel utilised in the event of a discrepancy, and with how many panellists?
- The NREC-MD noted that Table 7 (page 45) documents a list of the safety reporting requirements per country participating in the study, including the named National Competent Authority and contact details for reporting. The Committee requests clarification as to the omission of the Republic of Ireland from the table.

NREC-MD Application Form

The NREC-MD noted that the document requires additional information/amendments. The Committee requests that a revised copy be submitted, with updates at applicable sections:

- E4: The NREC-MD noted that both treatment arms of the clinical trial Cambria-2 may be administered with/without abemaciclib. The Committee seeks clarification, for information purposes, whether Ki67 status per the diagnostic will be a deciding factor in the decision to administer abemaciclib.
- K8, K9: Please provide additional information or N/A as applicable.

23-NREC-MD-038

- 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, Belfield, Dublin 4, Ireland
- NREC-MD Decision
  - *Request for further information*
- Further information requested

NREC-MD Application Form

The NREC-MD noted that the document requires additional information/amendments. The Committee requests that a revised copy be submitted, with updates at applicable sections:

- F3: Please update this section to clarify whether participants will be primigravida or multiparous. Please comment on whether the type of pregnant participant (primigravida vs. multiparous) has been considered in relation to their perception of fetal movements.
- F3: Please comment on how data will be processed/managed if more than the targeted 30 participants complete to 40 weeks/livebirth.
- F5: Please give additional information with regard to the logistical arrangements of the study team, and how those arrangements will impact recruitment and consenting of participants.
- F7: The applicant has indicated that identification of potential participants will not involve access to identifiable information. Please confirm and amend the application form accordingly.
- F10: Please provide an in-depth justification for the exclusion from the dataset of data from stillbirths. If data is excluded, how will this situation be handled e.g. removal of the device etc.? If excluded, will any portion of the data prior to stillbirth be used e.g. via interim reporting?
- F11: The NREC-MD noted the below statements with regard to potential benefits for participants in the study and for future users of the device. The Committee found these statements to be misleading and noted that the data generated has the potential to help develop algorithms which could illustrate 'normal' data/expectations for fetal movement. Moreover, the Committee requested that the aims/objectives and/or potential study outcomes be updated where they do not appear to align e.g. E3 conflicts with F11. Please update all relevant documentation (e.g. application form, PIL) to accurately reflect the aims/objectives and/or potential study outcomes of the study.
    - "Patients would have fewer out-patient appointments for fetal monitoring…"
    - "There is the potential for the device to reduce stillbirth rates…"
- F16, F17: Has due consideration been given to the aspects of the study which have the potential to induce anxiety, such as logging fetal movements, and how they might impact on the participant's overall experience of pregnancy? The NREC-MD suggests that an expert in clinical psychology be given the opportunity to comment.
- F16, F17: It is noted that "….participants will be more aware of their baby's movements". It is not clear whether this will be a positive or negative experience for pregnant participants. Please comment on the availability of literature which supports this. As the device is not a regular part of care or pregnancy experience, due consideration should be given to the potential impact on the pregnant participant/pregnancy experience. For example, if fetal movements are perceptively reduced on one day compared to another when monitoring, will the participant be advised to seek assistance, and from whom?

- F21: Please clarify why neither the participant's GP nor Consultant will be informed about their involvement with this study. The NREC-MD suggests that they should be notified.
- G10: Please provide information in relation to the procedure for recruitment and informed consent for the study. Please take into consideration and comment on the impact which anxiety may have on participants (including reference to primigravida vs. multiparous participants).
- H2: Please provide information in relation to the accommodations which might be made for participants who might not adequately understand verbal or written information.
- K4: Please comment on whether the Data Protection Officer of the National Maternity Hospital (NMH) has been given the opportunity to review and approve the involvement of the university located in Bangladesh, India. Please provide additional information with regard to transfer of data and training of the team.
- S1, S2: While the NREC-MD does not stipulate exact stipend/payment rates, it advises that every effort should be made to reimburse participants for reasonable expenses which may be incurred during study visits such as parking, refreshments etc. The Committee requests that the availability of such reimbursement be included in the Participant Information Leaflet.

Participant Information Leaflet and Informed Consent Form (PIL/ICF)

- With regard to the future use of pseudonymised data as outlined in the PIL, please ensure that the PIL and informed consent form (ICF) are in compliance with data protection regulations and legislation, including the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), 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.

Suitability of the Principal Investigator (PI)

- The NREC-MD noted that the National/Coordinating Principal Investigator for the study (application form, B1) and the Principal Investigator at the study site (application form, C3) will be different individuals. As the proposed study will be single-site only, please amend the submitted document(s) or provide the Committee with confirmation of the rationale for this difference.

Insurance & Financial Arrangements

- The NREC-MD noted that the study budget contains an allocation for the Principal Investigator (PI). Please confirm if this refers to the National PI, site PI, or both, and provide a justification for the monetary value.
- The NREC-MD noted that the Clinical Indemnity Scheme applies to the clinicians on site at the National Maternity Hospital (NMH) to carry out the study. Please confirm that all additional applicable insurance policies are in place for the study.

23-NREC-MD-039

- 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 Decision
  - *Request for further information*
- Further information requested

NREC Application Form

The NREC-MD noted that the document requires additional information/amendments. The Committee requests that a revised copy be submitted, with updates at applicable sections:

- E4: The NREC-MD acknowledged that randomisation into treatment arms is not applicable to this study, however the Committee requests clarification with regard to how healthy volunteers will be selected for either blood sample or bone marrow aspiration.
- F13: Please provide additional information with regard to: how/by whom responses to the advertisement will be triaged; how/by whom the questionnaire will be administered; how/by whom the blood test will be organised; who will perform the bone marrow aspiration.
- F18: Please confirm the mechanism which will be in place to facilitate adverse event reporting in the event that a participant reports same to their General Practitioner (as per the PIL, section 6.0).
- G4: Please confirm that the individuals conducting recruitment and consenting will be either the Principal Investigator (PI) or an authorised designee of the PI (as per ISO 20916:2019), an individual who is a member of the investigating team and who is appropriately qualified under national law (as per Article 59(2)(c) of the In Vitro Medical Device Regulation (EU) 2017/746).
- K15: This section indicates that data will be anonymised while Section L16 (d) and other submitted documents state that data will pseudonymised - please clarify and amend as applicable. Note that samples are considered to be data.

- K21: This section indicates that personally identifiable data of potential participants will be accessed by the Sponsor through healthcare records. Please clarify, since the study proposes to recruit healthy volunteers only.
- N1: Please clarify the response given in this section with regard to the potential for the human biological material obtained in this study and/or the data derived from the analysis of that material to be/to become commercially valuable.

Clinical Research Form (CRF)

- The NREC-MD noted the following item, to be answered yes/no, in the clinical research form (CRF). The Committee requests clarification and amendment to the CRF as applicable, for the purposes of maintaining participant safeguards associated with the quality of data which will be collected in the study.
  - "Presence or absence of haematological abnormalities"

Participant Information Leaflet/Informed Consent Form (PIL/ICF)

The NREC-MD noted that the document requires additional information/amendments. The Committee requests that a revised copy be submitted, with updates at applicable sections:

- Preamble: Please clarify that participants will not be required to engage/have involvement in the study for the duration of a twenty-four (24) month period, as could be inferred.
- 2.0: Please simplify the language used in the technical device/cytometry description and outline of the sampling method. The applicant may consider using images and/or flow charts to aid understanding by the participant.
- 2.0: Please provide additional justification for the decision not to provide participants (all of whom will be healthy volunteers) with accidental findings which may arise as a result of the performance testing of the diagnostic device. Please further comment on the decision not to forward such accidental findings to an appropriately accredited laboratory for confirmatory testing.
- 3.0: The PIL shows evidence of use for patients and has not been adequately edited for healthy volunteers. Please edit throughout to remove, for example, reference to 'medical records' (this section), 'alternative treatments available for my illness', 'further medical treatment' (ICF, page 12) etc.
- 3.0: Please clarify the below statement, bearing in mind that participants will be healthy volunteers recruited from amongst a student body population, who may not have medical records on file at Galway University Hospital. (See also K21: NREC-MD application form)
  - "After this form has been signed, your study doctor will assess if you meet all the requirements for participation based on the information present in your medical records, if applicable".
- 3.0: Please outline the rationale for the viral screening of blood samples and, if the rationale is to ensure that the applicable viruses are not present in bone marrow samples, please include a brief statement in the PIL/ICF to this effect.

- 3.0: Please outline the clinical referral pathways which will be in place and confirm that the appropriate supports will be available to prospective participants in the event that they receive a positive test result following viral screening of blood samples.
- 6.0: Please add clarity to the instructions for seeking treatment in the event that the participant feels unwell following bone marrow aspiration.
- 6.0: With regard to the below statements, the risks associated with the study procedures (blood draw and bone marrow aspiration) have been presented as almost equivalent. Bone marrow aspiration is a more invasive procedure, is likely to be less familiar to the participant, and is associated with a greater risk of pain. The Committee requests that the possibility of pain is highlighted more clearly, and suggests that the associated risks be quantified to increase transparency (e.g. 1 in 10, 1 in 100 etc…).
  - "The most common side effects of the blood collection by venipuncture include the following: pain, bruising or hematoma at the site of puncture, very rarely infections or nerve injuries might happen at the injection site…"
  - "The most common side effects of the bone marrow aspiration include the following: pain, bruising, hematoma or bleeding at the site of puncture, very rarely infections or nerve injuries might happen at the injection site…"
- 12.0: Please also include reference to the physical examination when outlining the procedures included in the study, at the applicable section.

Recruitment Material

- The NREC-MD noted that an advertisement/poster will be used for recruitment. The Committee requests that the poster clearly identifies that the study is in collaboration with the Sponsor.

Agreements

- The NREC-MD noted that the Principal Investigator regularly avails of the services of the diagnostic haematology laboratory in University of Galway for diagnoses and follow-up of patients. The Committee requests clarification as to whether Service Level Agreements are in place between the laboratory and the Sponsor.

Facilities/Site Suitability Form

- The NREC-MD noted that the one-time bone marrow sample collection via needle aspiration will take place at the 'Clinical Research Facility - University of Galway'. The Committee requests confirmation that the site is suitably equipped to facilitate aseptic procedures and local anaesthetic. Please confirm that the Principal Investigator will assume the applicable oversight role with regard to staff training on standard operating procedures (SOPs).

Budget:

- The NREC-MD noted that a breakdown of study costs is included in the Clinical Study Agreement (Exhibit A; Study Budget & Payment Schedule) in addition to the submitted itemised budget. The Committee requests clarification as to the following; the laboratory which will perform testing of the blood samples (and the cost/participant); the laboratory which will perform testing of the bone marrow samples (and the cost/participant).

Data Protection

- The NREC-MD noted that participants (all of whom will be healthy volunteers) will not be notified in the event that Multiple Myeloma is detected in their sample(s). Has the applicant given consideration to confirmatory testing of such samples in a suitable laboratory with CE-marked instrumentation, and applicable follow-up with participants?

23-NREC-MD-015-SM1

- Principal Investigator: Prof. Jarushka Naidoo
- Study title: Diagnostic Protocol for VENTANA PD-L1 (SP263) CDx Assay in Arcus Biosciences Study ARC-10
- Lead institution: Beaumont Hospital, Beaumont Road, Beaumont, Dublin 9, Ireland
- NREC-MD Decision
  - *Request for further information*
- Further information requested
    - The NREC-MD seeks additional reassurance that appropriate mechanisms are in place through which participants will be kept informed about applicable Adverse Events and Adverse Device Events. The Committee requests a brief outline of these mechanisms including reference to local protocols.

22-NREC-MD-036-SM3

- 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, Newcastle Rd, Galway, H91 YR71
- NREC-MD Decision
  - *Favourable*

23-NREC-MD-010-SM2

- Principal Investigator: Dr Darren Mylotte
- Study title: Evolut™ EXPAND TAVR II Pivotal Trial
- Lead institution: University Hospital Galway, Newcastle Rd, Galway, H91 YR71
- NREC-MD Decision
  - *Favourable*

23-NREC-MD-018-SM1

- Principal Investigator: Dr Ken McDonald
- Study title: First in Human Clinical Investigation of the FIRE1TM System in Heart Failure in Patients
- Lead institution: St. Vincent's University Hospital, Elm Park, Dublin 4, Ireland
- NREC-MD Decision
  - *Request for further information*
- Further information requested
  - The NREC-MD noted that the three-month blinding period which was in place at the outset of the study will be removed. The Committee requests a justification for this change and, in particular, responses to the below queries:
    - Please clarify why access to the initial three months of data would be helpful or relevant to the Principal Investigator (PI).
    - As the rationale for introducing the three-month blinding period was to reduce the risk of bias, please clarify how that risk has changed. How will the issue of bias in interpreting results be addressed?
    - What will be the resultant change in the risk/benefit profile to the participant of this modification?
  - The NREC-MD noted that the change to the inclusion criteria is intended to 'expand the pool of patients' (per the submitted cover letter). Putting the implant in patients who have are less comorbid will mean the implant will be expected to remain in patients for a longer duration. The last version of this implant had problems fracturing and a rationale for the longer device lifetime must be provided.
  - The NREC-MD request clarification and comment as to whether consideration has been given to safety mitigations, such as the use of stopping criteria, in the event that further device fractures are identified in Gen2.
  - PIL (page 1, 2): The NREC-MD noted that Section 2 of the PIL is the only place in which the Gen1 implant is mentioned. Please remove potentially leading language from Section 2 such as; "Learnings from the use of…", "… including evidence of device fractures…" and "design enhancements".

- PIL (page 2, 11): Please include direct language and an explanation for the layperson of a “device fracture”.

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- Principal Investigator: Prof. Gerry O'Sullivan
- Study title: Gore VIAFORT Vascular Stent VNS 21-05
- Lead institution: University Hospital Galway, Newcastle Rd, Galway, H91 YR71
- NREC-MD Decision
  - *Request for further information*
- Further information requested
  - The NREC-MD requests confirmation that applicable safety monitoring reports have been submitted to the Health Products Regulatory Authority (HPRA).

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