NATIONAL OFFICE FOR RESEARCH ETHICS COMMITTEES

National Research Ethics Committee

NREC-MD Meeting Minutes

18th April 2024

Attendance

Name	Role
Prof. Barry O'Sullivan (Chair)	Chair, NREC-MD
Prof. Mary Sharp (Deputy Chair)	Deputy Chair, NREC-MD
Dr Mireille Crampe	Deputy Chair, NREC-MD
Dr Ruth Davis	Member, NREC-MD
Dr Owen Doody	Member, NREC-MD
Dr Frank Houghton	Member, NREC-MD
Ms Orla Lane	Member, NREC-MD
Mr Billy McCann (PPI)	Member, NREC-MD
Dr Sarah McLoughlin (PPI)	Member, NREC-MD
Dr Declan O'Callaghan	Member, NREC-MD
Dr Paul O'Connor	Member, NREC-MD
Mr Damien Owens	Member, NREC-MD
Prof. Anne Parle McDermott	Member, NREC-MD
Prof. Mahendra Varma	Member, NREC-MD
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
Dr Lucia Prihodova *	Programme Manager, National Office for Research Ethics Committees
Dr Louise Houston	Project Officer, National Office for Research Ethics Committees
Dr Emily Vereker	Head, 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: Prof. Declan Patton, Dr Caitriona Cahir, Dr Gloria Kirwan, Prof. Tom Melvin, Prof. Therese Murphy, Prof. Susan O'Connell, Dr Clare O'Connor, Ms Riona Tumelty, Mr Peter Woulfe

Quorum for decisions: Yes

Agenda

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

New applications:

5. 24-NREC-MD-011
6. 24-NREC-MD-012
7. 24-NREC-MD-012 (resubmission of previously unfavourable 23-NREC-MD-039)
8. 24-NREC-MD-013
9. 24-NREC-MD-014

Substantial modifications:

10. 22-NREC-MD-003-SM4

11. AOB

- The Chairperson welcomed the Committee and acknowledged apologies sent and opened the meeting.
- NREC Committee Business Report: The Committee noted the report.
- Minutes of the previous meeting(s) (21st March 2024) were approved.
- Matters arising from the previous meeting: none
- Declarations of interest:
  - Mr Damien Owens (22-NREC-MD-003-SM4) did not read the documentation associated with the applications and vacated the meeting while the study was under discussion.

Applications

24-NREC-MD-011

- Principal Investigator: Dr Noel Horgan
- Study title: A Phase 3 randomized, masked, controlled trial to evaluate efficacy and safety of belzupacap sarotalocan (AU-011) treatment compared to sham control in subjects with primary indeterminate lesions or small choroidal melanoma.
- Lead institution: Royal Victoria Eye and Ear Hospital, 61 Adelaide Road, Dublin, D02 XK51.
- NREC-MD Decision
  - *Request for further information*
- Further information requested

- The Committee noted that it is currently unclear from the application documentation submitted which laser (Quantel Medical Vitra Aura Laser and Modulight ML6710i Laser) is being used in this study on participants in Ireland and request confirmation on:
  - Which device will be used in this study for participants in Ireland.
  - Are both devices equivalent in terms of safety and functionality. If not, how will the choice of device used be made and how does this impact the statistical power of the study.
  - The Participant Information Leaflet (PIL) is updated to include all the above information.
- What clinical setting the laser will be used and what steps will be taken to minimise laser injury.
- What clinical setting the Microinjector will be used and who will be performing the procedure (including qualifications); e.g. a standard exam room, operating theatre, clean room, will there be air exchange etc.
- What sterilisation techniques will be used when performing the microinjector procedure; e.g. sterile gloves, gowns, drapes, masks, surgical caps etc.

- The NREC-MD requests that Section D8 (a) of the Application Form is updated to clarify the use of the Investigational Medicinal Product as part of the Clinical Trial of Investigational Medicinal Product (CTIMP) with the SCS Microinjector.
- What is the current standard of care for individuals with primary indeterminate lesions or small choroidal melanoma and whether the use of sham treatment is appropriate.
- Whether participants from the sham group will be undergoing all blood tests and fluorescein angiography associated with this study.
- Confirmation whether the lasers used in this study involve non-ionising radiation and update Section O of the application form accordingly.
- Confirmation whether the data or samples collected as part of this study will be used for future research and update the application form and corresponding patient facing material accordingly.
- How long the blood samples collected as part of this study will be stored and when they will be destroyed.
- The NREC-MD requests that all participant facing documentation, including the clinical trial CTIMPs PIL are provided. Furthermore, the Committee requests a comment whether one PIL should be used instead of two to prevent confusion.
- The NREC-MD requests that the description of the microinjection procedure be elaborated to include the below and any other relevant information.
- The Committee noted that there is currently no information on the use of a speculum which can be uncomfortable; potential pain associated with the procedure; or that the use of antiseptic drops can cause irritation to the cornea which can feel gritty post procedure and requests these are specified in the PIL.
- Additionally, the NREC-MD requests that the risks associated with this study and its procedures be elaborated, for example:
    - Posterior vitreous detachment can lead to retinal detachment and blinding which may require surgery to repair.
    - Any injection involving the eye can lead to endophthalmitis which can also cause blinding.
    - Periocular or ocular injection can cause corneal abrasion which can be extremely painful.
    - Macular oedema which could potentially require steroid treatment in the form of ocular injection or systemic tablets.
    - The Fluorescein angiography procedure and the associated risks have not been adequately described.
- The NREC-MD noted that four participants will be recruited in Ireland and there is a potential that two (50%) participants will be in the sham group and requests this is included in the PIL.
- The risks associated with being on the sham treatment, if any, for the duration of the study should be included in the PIL..

- The NREC-MD requests a clarification on the recruitment and consenting process, who will be approaching potential participants, their qualifications, and on any procedures which will be in place to minimise any bias posed by the recruitment process.
- The NREC-MD requests that participants will be given a minimum of 24 hours to consider their participation in the study.
- Section F6 of the Application Form references recruitment tokens of appreciation. The Committee requests a clarification on what these are and their monetary value.
- The NREC-MD noted that participation in the study is enormously time consuming and requests that reasonable participant expenses, including lost wages, be reimbursed.
- The NREC-MD noted that participants will not be involved in any other research study and requests this is added to the study inclusion/exclusion criteria.The NREC-MD noted that participants will not be involved in any other research study and requests this is added to the study inclusion/exclusion criteria.
- Confirmation that site approval will be granted prior to initiating the study.
- The data collected is referred to as both anonymous and pseudonymous. However, it appears to be pseudonymous. Please clarify and update the documentation accordingly.
- Clarification on the arrangements in place to anonymise, archive or destroy the data once trial is complete.
- In Section K5 of the Application Form, confirmation on who the vendors are.
- In Section K16 of the Application Form, confirmation on which staff / personnel from 'The Site' will retain the key / master list which may be used to re-identify the data.
- In Section K17 of the Application Form, confirmation on who the delegated study site personnel will be.
- The NREC-MD noted that study data and files will be returned to the sponsor at the end of the trial. Please confirm what form this data will be in i.e. anonymous, pseudonymous. Section K20 of the application form states that "To ensure that personal information is kept confidential, patients' name and any other information that allows identification directly will not be entered in any records or samples provided to Sponsor or Sponsor's authorised representatives". However, Section K21 contradicts this. Please clarify this discrepancy.
- The Committee noted that any future research using anonymised data from the current study is subject to appropriate participant consent being in place as well as a favourable review from a Research Ethics Committee.

24-NREC-MD-012

- 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 assay.
- Lead institution: Galway University Hospital, Newcastle Road, Galway, H91YR71.

- NREC-MD Decision
  - *Request for further information*
- Further information requested
  - The Committee noted that only participants donating blood marrow will undergo screening blood draw. Please provide rationale for this approach, especially if presence of certain viruses or coagulopathies has impact on inclusion/ exclusion from the study.
  - The Committee noted that participants can enrol in the study more than once and requests clarification on the following:
    - Does repeated donation reduce biological replicates?
    - Can participants donate blood marrow more than once? If yes, does repeated blood marrow donation have any potential long-term implications for participants, should they need to undergo blood marrow investigational procedure or wish to be a donor for blood marrow transplantation, as blood marrow donation in previous 12 months is an exclusion criterion.
  - The Committee noted that there could be a delay of 45 days between screening and donation and requests a clarification.
  - The Committee noted that participants who report to be pregnant are excluded from the study and requests that for participants donating blood marrow a routine urine pregnancy test is carried before the procedure.
  - The Committee noted prospective participants who have undergone mastectomy are excluded from peripheral blood sampling and requests justification. If this is due to a risk of auxiliary clearance, the Committee queries whether auxiliary clearance should be the exclusion criterion rather than mastectomy. Furthermore, please clarify if the same exclusion criterion should also apply to blood marrow donation.
  - The Committee requests that “male or female subjects” is removed from the inclusion criteria throughout to promote inclusive terminology.
  - The Committee noted that the process of responding to the advertisement has not been appropriately described and requests clarification.
  - The Committee noted that it is not clear who will consent participants and requests clarification on the individual’s qualifications.
  - The Committee requests that the PIL/ICF is revised to minimise technical language to increase accessibility. It was noted that an inclusion of flow diagram visualising the study process might be beneficial.
  - The Committee noted that there is already a kit available for diagnosing multiple myeloma and requests that it is made clear in the participant facing documentation.
  - Point 8 on “are there any extra costs” also includes information about compensation. The Committee requests that information on compensation is provided separately.
  - The Committee noted that study participation finishes at the time of donation. In the case of bone marrow sampling, please clarify how delayed procedure-related adverse events (such as infection or haemorrhage) will be captured. Please consider whether

participants should be closed out from the study 7-14 days after procedure rather than at the time of donation.

- The Committee requests clarification on whether the study PI is best placed to provide aftercare to participants experiencing adverse events.
- The Committee requests a specific GP letter to be designed for participants undergoing blood marrow donation and experiencing side effects.
- The Committee noted that the process for incidental findings from is well described in the cover letter and requests it is also included in the protocol and participant information leaflet.
- However, the Committee requests clarification on the process of reporting incidental findings from analyses carried out in BD labs.
- The Committee noted that there is lack of clarity on what study procedures, tests and analyses are carried out where in CRF Galway, Galway University Hospital and in BM and request clarification. Additionally, please clearly outline the responsibilities of each.
- The Committee requests more details on the suitability of the site facilities, including on what equipment and personnel will be made available for the study. Alternatively a copy of accreditation status to the ISO 20916 standards and certificate of adherence to GCP should be provided.
- The Committee noted that the study is likely to run over the duration of the insurance certificate and requests a confirmation it will be extended as appropriate.
- Section S1 of the Application form states that “Each subject, who signed the Informed Consent Form will receive € 20.” To minimise any undue influence, the Committee requests that reimbursement is provided for completion of screening visit instead.

24-NREC-MD-013

- Principal Investigator: Prof. Jarushka Naidoo
- Study title: DIAGNOSTIC DEVICE CLINICAL STUDY PROTOCOL, Performance of VENTANA PD-L1 (SP263) CDx Assay with OptiView DAB IHC Detection on the BenchMark ULTRA Instrument to Determine the PDL1 Expression Level of Non Small-Cell Lung Cancer (NSCLC) Specimens for Roche Phase III Study GO45006.
- Lead institution: Beaumont Hospital, Beaumont Road, Dublin 9, D09 V2N0.
- NREC-MD Decision
  - *Request for further information*
- Further information requested
  - The Committee noted that in its current form the application documentation does not clearly lay out the clinical performance study (CPS) procedures. The Committee requests that applicants give due consideration on the information on the CPS as opposed to Clinical Trial of Investigational Medicinal Product (CTIMP) in future ethics applications for similar studies.

- The Committee noted that as such the CPS per se is not being conducted in Ireland and that no information on the pathology laboratoriess where testing and analysis is performed is provided.
- Furthermore, the Committee noted that there are discrepancies across the application documentation on where the samples will be tested. To that end, please provide an exhaustive list of countries and laboratories in which the samples will be processed and stored. Please also provide details on the certification/ accreditation to recognised quality standards of any laboratories or storage facilities utilised as a part of this study.
- The Committee noted that the NREC-MD application form lists several data processors, eg LabCorp and CellCarta, Almac iMedidata, Clario, etc but it is not clear where they are located and what role each of these has in the CPS. Please provide a clarification.
- The Committee noted that no DPIA was provided and no Irish Data Protection Officer has had an input into the DPIA. Please provide a copy of CPS related DPIA or a statement of compliance related to same. Furthermore, please provide assurance that the site DPO feedback will be obtained before the study commences.
- The Committee noted that NREC-MD application form and overall clinical trial protocol indicate that part of the screening includes testing for HIV, Hepatitis, etc, however no information on such testing is included in the pre-screening consent form and instead this information is in the main study ICF. The Committee requests clarification on whether the information should be included in pre-screening consent form?
- The Committee noted that samples will be destroyed 5 years after final study results, with the exception of samples for biomarker testing which will be stored for 10 years after the final study results have been reported. The Committee request clarification on what type of biomarker studies does this refer to. Furthermore, if any samples and data are retained for future research, separate informed consent for such must be sought. Please note, future studies would also be subject to review by a research ethics committee.
- The Committee noted that samples will be tested for EGFR/ALK mutations and requests clarification on where will this be done and how will this data be shared? Please also comment on what assurances can be provided to ensure these patients are managed appropriately given they cannot participate in the trial.
- Further to previous point, the Committee requests clarification on how will incidental findings be handled.
- The Committee noted that the PIL/ICF uses technical terminology and requests that it is revised extensively to ensure accessibility. The Committee noted that a study summary at the beginning of the PIL/ICF might be beneficial.
- Furthermore, the Committee noted that some sections of the pre-screening PIL/ICF provide information more relevant to the CTIMP rather than the CPS, eg Section 1.9 What happens if I am injured?
- The Committee requests that the risks of false positives/ negatives are outlined in the PIL/ICF (Section 2.1 Risks), as well as any implication of participant being put onto

the investigational clinical drug because of a false positive screening test, such as side effects, toxicities, etc.

- The Committee noted that the informed consent form (ICF) for the pre-screening alone leaves out some relevant information in relation to the ctDNA and Research Biosample Repository (which are mentioned in the main application form) and noted that it is not clear that the PD-L1 test is carried out for as a part of screening for the trial and the ctDNA and RBR tests are carried for further research/knowledge generation. The Committee requests this is clarified and laid out in a format that allows the participants to know upfront that there are a number of separate consents being asked.
- The Committee noted that in its current form, it is not clear that EGFR/ALK testing is genetic testing and requests this is clearly outlined.
- The Committee requests that the PIL and ICF are separated into two documents.
- The Committee noted that the information on reimbursement in the NREC-MD application form relates to the CTIMP rather than the CPS and requests clarification.

24-NREC-MD-014

- Principal Investigator: Dr Niamh Hynes
- Study title: Stagewise assessment of the ability of venous leg ulcer patients and nurses to utilise pressure monitoring technology for improving the targeted application, monitoring, and maintenance of compression therapy.
- Lead institution: Galway Clinic, Doughiska, Galway, H91 HHT0.
- NREC-MD Decision
  - *Favourable with conditions*
- Associated conditions:
- Study participants and recruitment
  - No sponsor associated staff are permitted to be participant in the study.
  - In the interest of equitable access to research participation, all reasonable efforts should made to allow access to the study for participants without proficient English, or who do not speak English. Such participants should be provided with a copy of a translated Participant Information Leaflet and Informed Consent Form and the translations must be completed by a certified translation provider. Copy of translation certificates should be provided to the National Office as non-substantial amendment. In addition, when interacting with the study team, the services of interpreter should be made available to such participants.
  - Participant recruitment and any study related procedures to be performed by a suitably qualified member of the study team who is not involved in direct health care for the participant nor are related to the study sponsor. The information on the qualifications of the appointed individual to be provided to the National Office.

- Confirm how the healthy volunteer will be recruited.
- Justification for the exclusion of pregnant / breastfeeding participants and participants of childbearing potential. All reasonable efforts should be made to include these populations in this study.
- Confirm how wound healing will be assessed. Will this be solely based on clinician judgement, which can lead to judgement bias, or is there an additional measure e.g. photographs. If using photographs or other methods, this must be included in the Participant Information Leaflet (PIL).
- Confirm how the eKare software will be used. Is this standard of care practice? What data will the software have access to and how will data be processed.
- Participant's GP to be informed of their patient's participation in the clinical investigation. Participant's consent to share the information on their participation with their GP should be sought and a copy of the letter sent to the GP should be provided to the National Office.
- The Committee noted that the study protocol in its current form does not confirm with the ISO 14155/2020 and requests future protocols are drawn up as per ISO 14155/2020.
- The Protocol is updated to include the maximum and minimum number of participants to be recruited for this study.
- The Protocol and Case Report Form is updated to include more information on Venous Leg Ulcer healing rates. Confirm how you propose to measure the wound size (in units). Include a definition and the method of wound size measurement.
- The nurse participant PIL is updated to include the risks associated with a healthy nurse using this device rather than a patient participant.
- The nurse participant PIL is updated to remove reference of the Principal Investigator having access to their medical records.
- The PIL to include an outline of what how participant data will be processed if they withdraw from the study.
- All reasonable participant expenses be reimbursed. All compensation should be outlined in the PIL.
- Option 4 is removed from all PILs in the section "STORAGE AND FUTURE USE OF INFORMATION".
- With regard to the future use of data as outlined in the PILs (Option 3 in the Informed Consent Form (ICF)), please ensure that the PIL and 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.

- Confirm if all participants, including the healthy volunteer and carers will receive a €50 one for all voucher as per other study participants.
- A device card is provided to participants in case they are required to travel during their participation.

- **22-NREC-MD-003-SM4**
- Principal Investigator: Prof. Faisal Sharif
- Study title: Global SYMPLICITY Registry (GSR) Denervation Findings in Real World (DEFINE) is referred to as the GSR DEFINE study, Including Irish Country Addendum (IMPROVE).
- Lead institution: University Hospital Galway, Newcastle Road, Galway, H91 YR71.
- NREC-MD Decision
  - *Favourable*

AOB

- The Committee requested a discussion to be held at future meetings on the topic of access to participation and provisions for participants who are not fluent in English.
- The Chairperson thanked the Committee and closed the meeting.