NATIONAL OFFICE FOR RESEARCH ETHICS COMMITTEES

NREC-MD Meeting Minutes

15th May 2025

Attendance

Name	Role	Attendance/ Apologies
Prof. Barry O'Sullivan	Chair	Attended
Prof. Mary Sharp	Deputy Chair	Attended
Prof. Declan Patton	Deputy Chair	Attended
Ms Alyson Bailey	Member	Attended
Dr Caitriona Cahir	Member	Attended
Dr Daniel Coakley	Member	Attended
Dr Mireille Crampe	Member	Attended
Dr Ruth Davis	Member	Attended
Dr Owen Doody	Member	Apologies
Prof Roisin Dwyer	Member	Apologies
Dr Frank Houghton	Member	Attended
Dr James Gilroy	Member	Apologies
Prof Suzanne Guerin	Member	Attended
Dr Gloria Kirwan	Member	Apologies
Ms Orla Lane	Member	Attended
Prof. Cara Martin	Member	Attended
Mr Billy McCann (PPI)	Member	Attended
Dr Natalie McEvoy	Member	Apologies
Prof. Tom Melvin	Member	Attended
Prof. Therese Murphy	Member	Apologies
Dr Declan O'Callaghan	Member	Attended
Dr Clare O'Connor	Member	Attended
Prof Paul O'Connor	Member	Apologies
Dr Joanne O'Dwyer	Member	Attended

Mr Damien Owens	Member	Attended
Prof. Mahendra Varma	Member	Apologies
Mr Peter Woulfe	Member	Apologies
Ms Simone Walsh	Member	Attended
Louise Houston	Project Officer, National Office for Research Ethics Committees	Attended
Dr Sarah McLoughlin	Programme Officer, National Office for Research Ethics Committees	Attended
Dr Lucia Prihodova	Programme Manager, National Office for Research Ethics Committees	Attended
Dr Emily Vereker	Head of Office, National Office for Research Ethics Committees	Apologies
Ciaran Horan*	Administrative Assistant, National Office for Research Ethics Committees	Apologies

Quorum for decisions: Yes

Agenda, discussion and decisions	
1. Welcome and apologies	The Chairperson welcomed the Committee, acknowledged apologies and opened the meeting.
2. Report on Committee business	Noted
3. Minutes of previous meeting	Adopted
4. Declarations of interest	Member Name: Mr Damien Owens Applications: 25-NREC-MD-005-R2, 25-NREC-MD-006-R2 and 24-NREC-MD-022-SM1 Mr Owens stepped out of the meeting for the discussion of the application.

5. 25-NREC-MD-005-R2	• Principal Investigator (Lead Institution): Prof Faisal Sharif (University Hospital Galway) • Sponsor: Medtronic Vascular, Inc • Study title: Spyral InSight Early Clinical Feasibility Study • NREC-MD decision: Favourable
6. 25-NREC-MD-006-R2	• Principal Investigator (Lead Institution): Prof Faisal Sharif (University Hospital Galway) • Sponsor: Medtronic Vascular, Inc • Study title: SPYRAL GEMINI Pilot Study • NREC-MD decision: Request for further information • Further information requested: – Prospective participants need to be able to make a decision about their participation based on the information being presented to them in the PIL/ICF. The NREC-MD noted that while information requested to be added to the document in the previous request has been added, this important information is briefly mentioned within dense text. – The Committee further noted that the PIL/ICF is far too long, and in its current format not a suitable tool to get truly informed consent for a study of such magnitude and potential risks. The Committee also noted that the sponsor refused to revise the PIL/ICF into separate documents for the 'on-med' group and the 'off-med' as requested by the Committee. Therefore, the NREC-MD requests that: – The PIL is extensively revised for accessibility – The PIL is reduced in length. This can be facilitated by creation of separate PILs for the two treatment groups as previously requested. – If the revised PIL cannot be reduced in length, a summary PIL must be developed in line with the National Office Guidance: https://www.nrecoffice.ie/pil-summary-guidance/ – The opening paragraph of all participant facing documentation must highlight the experimental nature of the study, in particular that: ○ Hepatic denervation is a new and experimental procedure ○ That the impact of hepatic denervation beyond 1 year is currently unknown. Therefore, it is not clear what is the long-term impact of hepatic denervation not just on

	hypertension, but also on the function of all organs that will be affected by the procedure (list all organs that might be affected as a consequence of the procedure to the hepatic artery). o The catheter used for the hepatic denervation is being used outside its approved use/ CE marking. – The NREC-MD noted that the Sponsor is liaising with the site in relation to obtaining approval by the Chairperson of the Radiation Safety Committee. If the approval is granted in the meantime, the Committee request evidence of this approval is included with the response.
7. 25-NREC-MD-009-R1	• Principal Investigator (Lead Institution): Dr Sebastian Trainor (Tallaght University Hospital) • Sponsor: Bristol-Myers Squibb Company • Study title: Clinical Performance Study Protocol for Use of the VENTANA PD-L1 (SP263) CDx Assay: Evaluation of PD-L1 Expression Levels in Non-small Cell Lung Cancer Specimens from Phase III Study CA2241093 (Relativity 1093) • NREC-MD decision: Favourable with conditions • Associated conditions: – In relation to the samples sent from the study sites, the NREC-MD requests that slides are to be sent instead of FFPE block whenever feasible. – The Participant Information Leaflet is revised to highlight that the sponsor is seeking to retain participant samples which otherwise might be an important source of information for future treatment. – A specific consent line must be included in the Informed Consent Form for participants to indicate their consent with retention of their samples. – Samples of participants of the performance study who are deemed not eligible for enrolment in the clinical trial shall be returned to the site.
8. 21-NREC-MD-003-SM2	• Principal Investigator (Lead Institution): Prof Patrick Serruys (University of Galway) • Sponsor: University Hospital Galway • Study title: Non-inferiority of angiography-derived physiology guidance versus usual care in an All-comers population treated with unrestricted use of Healing-Targeted Supreme stent (HT

	Supreme) and P2Y12 inhibitor monotherapy after 1-month of dual-antiplatelet therapy: the PIONEER IV trial • NREC-MD decision: Favourable
9. 25-NREC-MD-010	• Principal Investigator (Lead Institution): Prof Andrew Murphy (University Hospital Galway) • Sponsor: University Hospital Galway • Study title: A Prospective Evaluation of a Prescription Digital Therapeutic (PDTx) for Treatment of Overactive Bladder in Women: The RiSolve Trial • NREC-MD decision: Favourable with conditions • Associated conditions: – The NREC-MD noted that participants will need to "forego all other AOB treatments outside of the RiSolve for the trial treatment period" (inclusion criteria, CIP, page 7). However, the study protocol (page 26) states that 'concomitant medications', including 'a list of bladder medications' is documented. Clarify: o will participants have to stop all other OAB treatments for the duration of the study o who will be providing instruction to participants on their OAB medications over the duration of the study. – The NREC-MD requests that the question mark is removed from 'Amara Therapeutics?' on page 6 of the Participant Information Leaflet / Informed Consent Form (PIL/ICF). – The anticipated time commitment related to use of the app and study participation, (exercises, therapies and diaries), must be clearly laid out in the PIL/ICF. – While the NREC-MD noted that while the app will contain instructions for participants and a detailed instruction manual has been developed to assist with questionnaire completion, the participants are expected to independently review this large volume of information. The NREC-MD requests that participants are offered a consultation with an appropriate member of the study team to discuss study procedures, the app and the questionnaire completion throughout the study. – The NREC-MD requests confirmation that the app used for the study is self-contained and that cybersecurity of the app is periodically assessed. – The insurance policy is renewed for the duration of the study.

10. 25-NREC-MD-011	• Principal Investigator (Lead Institution): Dr Christina Fleming (University Hospital Cork) • Sponsor: Qufora • Study title: A randomized clinical investigation to assess efficacy of low volume Transanal Irrigation by Qufora® Irrisedo Minigo versus conservative treatment for Low Anterior Resection Patients • NREC-MD decision: Request for further information • Further information requested: – The NREC-MD noted that potential participants will undergo an examination to evaluate anastomosis and to exclude stenosis in order to determine their eligibility for the study. The NREC-MD requests clarification if this exam precedes consent and falls under standard or care. If this examination is study specific, then the Participant Information Leaflet / Informed Consent Form, (PIL/ICF) and other appropriate documentation should be updated accordingly. – The NREC-MD noted that the study utilises randomised design and this study intends to compare the device with standard of care however the NREC-MD Application Form (page 10/11) indicates that there is no control. Clarify this discrepancy and update the appropriate documentation accordingly. – The NREC-MD noted that section G9 of the NREC-MD Application Form states that participants will be encouraged to return to the clinic for an end of study treatment to ensure their safety. Clarify the risk to participants if they do not return and if applicable include it in the Participant Information Leaflet/ Informed Consent Form (PIL/ICF). – In order to understand the burden of time participants will have to dedicate to take part in the study, clarify the following and include in the PIL/ICF: o whether the study visits will be carried out together with routine clinical visits or as dedicated study visits/ participants will have a dedicated time to meet with the study team for review or if the visits will be done during standard of care visits, and o how long each study visit will be. – The NREC-MD requests confirmation if participants who do not speak English will be recruited. 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. If 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 noted that up to 50 participants will be recruited in Ireland, however both sites aim to recruit 5-10 participants. Clarify if the remaining participants will be recruited from additional sites, subject to substantial modification. - The NREC-MD noted that participants will be identified and approached by a member of the clinical team. However, it is unclear who exactly will be consenting participants. Clarify and note that in line with best practice there should be separation between clinical and research activities to minimise any confusion and perceived coercion. - The NREC-MD requests justification for the exclusion of pregnant / breastfeeding participants. - The NREC-MD requests that participants are given a minimum of 24 hours to consider their participation in the study. - The NREC-MD requests the PIL/ICF it is extensively revised to minimise technical language to increase accessibility as in its current form it is not accessible to a layperson. For example, the abbreviation LARS should be spelled out and explained to potential participants. If feasible, the revised PIL/ICF should be reviewed by a PPI group. - The PIL/ICF should be localised to Ireland, including contact details for the Irish Data Protection Commissioner. - The NREC-MD requests that it is made clear on page 1 of the PIL/ICF that previous use of the device excludes potential participants from taking part in the study. - The NREC-MD requests that the risks/ adverse events of participation in the study are quantified/ categorised based on risk and likelihood of occurrence. - The NREC-MD requests that the risks associated with other devices are not included in the PIL/ICF, where appropriate. - Further to point 4, the PIL/ICF should be updated to specify how long each study visit will take. - In line with Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018, the consent form needs to be

	revised to facilitate unbundled consent for each individual item. – The NREC-MD noted that the description of future research is very broad and requests it is revised. Consent for future use of data must be limited to a particular disease area or more generally in that area or a related area of health research and must be clearly described in the Participant Information Leaflet. An example would be limiting future use of study data to the disease and / or medicinal product / device being studied. Note that any such future studies are a subject to separate REC review. – The NREC-MD requests the consent information on future use of data is presented separately from the consent items for the main study as participant should be able to take part in the study and refuse the optional elements. – Section K11 and K12 of the Application Form must be completed. – The Committee requests confirmation that the applicant has engaged with the site Data Protection Officer (DPO) and that provide proof of engagement. – Section K15 of the Application form states that data will be pseudonymised, however the PIL/ICF states that data will be anonymised. Clarify this discrepancy and update the documentation accordingly. If data is to be anonymised a specific consent must be sought to facilitate this. – The NREC-MD requests clarification why data might be retained for longer than 15 years. – The NREC-MD noted that participants will be reimbursed for travel expenses. Section S1 of the Application Form should be completed. – The Committee noted that processing of expenses might pose unnecessary burden on study participants and requests a consideration is given to flat fee instead. – The NREC-MD noted that the insurance certificate submitted is for €5,000,000, which does not meet the requirements outlined in the State Indemnity Guidance: Clinical Trials Health Research and must be revised. – The NREC-MD requests confirmation that the insurance policy will be renewed for the duration of the study. – The NREC-MD requests clarification on any payments that the study site will receive for the study.

	– The NREC-MD requests confirmation of GCP training for Dr Hanley.
11. 25-NREC-MD-012	• Principal Investigator (Lead Institution): Prof Roisin Connolly (Cork University Hospital) • Sponsor: Fundacio de Recerca Clinic Barcelona-Institut D'Investigacions Biomediques August Pi i Sunyer (FRCB-IDIBAPS) • Study title: The DEFINITIVE Trial: Diagnostic HER2DX-guided treatment for patients with early-stage HER2-positive breast cancer. • NREC-MD decision: Request for further information • Further information requested: – The NREC-MD noted that from the submitted documentation it was not clear whether both components of the device – the software and the assays are investigational and subject of current performance study. Clarify and revise all documentation as appropriate. – The Committee noted the study aims to enrol participants presenting with early stage breast cancer and that the Application Form defines this as those presenting with Stage 2 / Stage 3a breast cancer. However, recent HSE guidance defines stage 3 as advanced cancer. Clarify this discrepancy and update all relevant documentation accordingly. – The Committee requests clarification on the termination criteria for the performance study. – The Committee noted that Section F15(a) indicates that no treatment would be withheld from participants as a result of taking part in this study. The Committee requests clarification on what actions will be taken if the software recommends withholding certain chemotherapy treatments if indicated by the algorithm. Clarify this discrepancy and update all relevant documentation accordingly if appropriate. – The NREC-MD noted that samples from participants will be retained after the study even if participants withdraw from the study. Justify. – The Committee requests clarification on how the blocks of tissue are selected and in what condition do the samples have to be to be considered eligible for the study. – The NREC-MD noted that the appendices in the 11. HER2DX_Investigators Brochure V5_05022025 that refer to the software are blank and request these are provided.

	- The NREC-MD requests clarification where is the software hosted and whether the software diagnostic analysis will take place in Ireland or Spain. - The NREC-MD also noted that there is a biobank in Spain included in this study. Clarify the role of this biobank in relation to patient samples. - Also provide details on the certification/ accreditation to recognised quality standards of any laboratories or storage facilities utilised as a part of this study. - Section F21 of the Application Form implies that the hospital consultant will not be informed of a patients/ participation in the study. However, the NREC-MD noted that the hospital consultant will be recruiting individuals into this study. Clarify this discrepancy. - The NREC-MD noted that anyone presenting with HER2+ breast cancer, meeting the inclusion criteria, can be recruited to this study. The Committee requests clarification on how recruitment bias for those the clinician deems to have a less severe form of the cancer will be avoided. - The NREC-MD requests due consideration is given to development of separate PIL/ICF for the performance study. - The NREC-MD requests the PIL/ICF is revised to include relevant contact information for participants from Ireland, eg the site data protection officer, the Data Protection Commissioner, etc. - The NREC-MD noted that the PIL/ICF states that the software is supported by “a large body of scientific evidence”. The Committee requests that this is expanded to include more detail about the scientific evidence supporting the device. - Additionally, the NREC-MD requests that the PIL/ICF be updated to include information about the development of the device. - The NREC-MD request the PIL/ICF is revised to highlight that the device is investigational and the associated risks with this. - Furthermore, the NREC-MD requests that the risks of false negatives and false positives and related consequences are clearly described in the PIL/ICF. - The Committee requests that the section on withdrawal from the study is made clearer so study participants know that

	while they will remain on their treatment course, the data surrounding quality of life will no longer be gathered. – The NREC-MD requests the PIL/ICF is updated to make it clear to participants that they will be provided a separate PIL/ICF to retain samples for future research. – In relation to 9. DEFINITIVE_FutureUse ICF_V1.0_060325_Cork_clean, the NREC-MD noted that page 3 appears to speak to incidental findings. The Committee requests clarification on the process of reporting incidental findings from analyses carried out on samples and that the process is clearly outlined in the participant facing documentation. – In relation to 9. DEFINITIVE_FutureUse ICF_V1.0_060325_Cork_clean, there is a consent line that refers to information that may be shared with participant/family. The NREC-MD noted that it is not clear what data/information is being referred to and request it is clarified. – The NREC-MD noted reference to Spanish Data Protection throughout the application (e.g. Section G3 and K19 of the Application Form). Confirm that the study will be carried out in accordance with the Irish Health Research Regulations (2018) and update the documentation as appropriate.
12. 25-NREC-MD-013	• Principal Investigator (Lead Institution): Prof Faisal Sharif (University Hospital Galway) • Sponsor: Endotronix, Ireland Limited • Study title: A Prospective, Multi-Center, Open Label, Randomized Control Clinical Trial Evaluating the Safety and Efficacy of the Cordella™ Pulmonary Artery Sensor System in New York Heart Association (NYHA) Class II - III Heart Failure Patients (PROACTIVE-HF-2 Trial) • NREC-MD decision: Request for further information • Further information requested: – The NREC-MD requests justification for not approaching participants who do not speak English, particularly as the study protocol notes that specific efforts will be made to include minorities. – 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. If 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 noted that a Patient Brochure and Patient Data Guide were submitted for review. Clarify the proposed use of these documents. – The NREC-MD requests a declaration of interest form be submitted for Dr Catherine Daly. – The PIL/ICF as it is currently written is overly technical and not accessible to a layperson. The NREC-MD request the PIL is shortened and revised to minimise technical language to increase accessibility. – Given the complex nature of the study and the volume of information in the PIL/ICF, the NREC-MD requests that a qualified member of the study team review the PIL with potential participants to ensure that the they understands all aspects of the study. – From the submitted documentation it appears that participant data is to be anonymised. In line with S.I. No. 314 of 2018 Data Protection Act 2018 (Section 36(2)) (Health Research) Regulations 2018 explicit consent is required for anonymisation. Revise the ICF accordingly. – Section O of the application form has not been fully filled out / completed e.g. O6. The NREC-MD requests that this section is reviewed to ensure all relevant information is present and section O28 of the Application Form is signed by an expert in radiation. – As identification of potential participants will involve access to identifiable information, section 7(b) of the Application Form must be completed. – The NREC-MD noted that participants will be reimbursed for out-of-pocket expenses such as travel and parking expenses. Given the commitment required during some of the study visits, the Committee requests that further consideration is given to whether the participants should be offered a payment for earnings lost or reimbursement for other expenses such as childcare costs.
13. 24-NREC-MD-022-SM1	• Principal Investigator (Lead Institution): Prof Andrew Sharp (Mater Hospital) • Sponsor: Medtronic

	• Study title: SPYRAL AFFIRM Global Clinical Study of Renal Denervation with the Symplicity Spyral Renal Denervation System in Subjects with Uncontrolled Hypertension (SPYRAL AFFIRM) • NREC-MD decision: Favourable with conditions • Associated conditions: – The Participant Information Leaflet / Informed Consent Form (PIL/ICF) to be updated to include the following: o The use of local anaesthetic is included in the description of procedures and tests for angiogram and renal denervation procedures, where appropriate. o NREC-MD will never request access to participant data. Remove reference to the ethics committee accessing participant data. o As data will be anonymised (as per page 16 of the PIL/ICF), the Committee requests that specific explicit consent for this is sought. o As data that will be sent outside the EU/EEA, the Committee requests that specific consent for this is sought. o The NREC-MD noted that the description of future use of data for the substudy differs from the one in the main study, and that in its current form is too broad. The NREC-MD requests the outline and consent item are revised in line with the ones in the main study. The NREC-MD advises the applicant that subsequent research ethics review must be sought for specific research once clearly defined.
14. 24-NREC-MD-007-SM1	• Principal Investigator (Lead Institution): Prof Raymond McDermott (Tallaght University Hospital) • Sponsor: Pfizer • Study title: An Open-label, Randomized, Controlled Phase 3 Study of Disitamab Vedotin in Combination with Pembrolizumab Versus Chemotherapy in Subjects with Previously Untreated Locally Advanced or Metastatic Urothelial Carcinoma that Expresses HER2 (IHC 1+ and Greater) • NREC-MD decision: Favourable
15. 23-NREC-MD-013-SM1	• Principal Investigator (Lead Institution): Prof James Loughman (Technological University Dublin) • Sponsor: CooperVision Manufacturing Ltd.

	• Study title: Children Myopia control Evaluation of Novel Soft Contact Lens Designs • NREC-MD decision: Favourable
16. 24-NREC-MD-011-SM2	• Principal Investigator (Lead Institution): Dr Noel Horgan (St Vincents Hospital) • Sponsor: Aura Biosciences • 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 • NREC-MD decision: Request for further information • Further information requested: – The NREC-MD noted the inclusion criteria has been expanded to increase the allowable tumour size (lesions in contact with the optic disc ≤ 7 clock hours (≤ 210 degrees) and Larger LBD of ≤ 12mm). The Committee noted this might increase the risk to participants and requests clarification on the following: o What clinical data has been used to support the decision to expand allowable tumour size. o Has there been a risk assessment conducted to support the expansion of the allowable tumour size. If so, provide details of this. If not, provide justification for this. – The NREC-MD noted that once participants are discharged from the trial, and if they provide a separate informed consent, they will be enrolled in a non-interventional, long term safety study. Clarify if this is a separate observational study after the trial or an extension of the current trial. – Additionally, while not subject of the current modification the Committee noted that the Participant Information Leaflet / Informed Consent Form (PIL/ICF) would benefit from addition of the following modifications to aid accessibility: o The risk of raised intraocular pressure and cataract (which may require surgical intervention) as a result of steroid use. o Clear definition what a sham procedure is so that participants understand unequivocally that no treatment will be given.

	○ Outline of what happens to participants in the sham group if the tumour size increases (e.g. they are offered treatment etc). ○ Information on how each of the study arms affect long term follow up e.g. frequency of visits, additional testing. A flow chart for each study arm may be useful here.
17. AOB	• None