NREC-MD Meeting Minutes

19th June 2025

Attendance

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

Prof Mahendra Varma	Member	Attended
Mr Peter Woulfe	Member	Attended
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	
5. 25-NREC-MD-006-R3	• Principal Investigator (Lead Institution): Prof Faisal Sharif (University Hospital Galway) • Sponsor: Medtronic Vascular Inc • Study title: SPYRAL GEMINI Pilot Study

	• NREC-MD decision: Favourable with conditions • Associated conditions: 1. The study is approved by the Galway Radiation Safety Committee following an independent and substantive review. 2. The insurance policy for this study specifically covers data breaches and damage to the participants smartphone should this occur in the process of investigating such a breach.
6. 25-NREC-MD-011-R1	• 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: Favourable
7. 25-NREC-MD-012-R1	• Principal Investigator (Lead Institution): Prof Roisin Connolly (Cork University Hospital) • Sponsor: Fundacio de Recerca Clinic Barcelona-Institut D'Investigacions Biomediques August Pi i • Study title: The DEFINITIVE Trial: Diagnostic HER2DX-guided treatment for patients with early-stage HER2-positive breast cancer. • NREC-MD decision: Favourable with conditions • Associated conditions: 1. In relation to point 2 of Decision letter 1, the terminology in the Participant Information Leaflet must be clarified to minimise confusion for the participants in Ireland who are familiar with the HSE terminology. The Committee noted that given the possibility of recurrence or death of people with stage 2-3 cancer it may not be appropriate to refer to these stages as 'curable'. 2. The Participant Information Leaflet must be revised to more factual language and any leading statements are removed. For example, "proving accuracy" is inappropriate given the investigative nature of the device. 3. In relation to incidental findings from future research for participants who indicate that they do not wish to be contacted about their results, the Committee had an extensive discussion about the proposed plan outlined in point 9 of the Response to Decision letter 1. As results of genetic testing might have implications, not just for the study participant but also their family,

	and the best practice in this area is continually evolving, the NREC-MD request that the plan outlined in the response is appraised with best ethical practice, applicable regulations and guidance in this area at the time. E.g. section 3.4.1 of the HSE National Policy for Consent in Health and Social Care Research.
8. 25-NREC-MD-013-R1	• Principal Investigator (Lead Institution): Prof Faisal Sharif (UHG) • 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: Favourable
9. 25-NREC-MD-014	• Principal Investigator (Lead Institution): Dr Patricia O'Connor (St James's Hospital) • Sponsor: Roche Diagnostics International Ltd • Study title: Measurement of Samples with Tina-quant Lp(a) RxDx to Identify Participants with Elevated Lipoprotein(a) for Prevention of First Major Cardiovascular Events • NREC-MD decision: Favourable with conditions • Associated conditions: 1. Site DPO input / feedback to be implemented prior to study initiation. 2. The NREC-MD requests that appendix A on page 11 of the PIL/ICF is moved to earlier in the document before the participant consent form. 3. The PIL/ICF as it is currently written implies that additional testing and future research may be carried out on participant samples. If future research is to be carried out, then this should be outlined clearly in the documentation and a specific consent line for this should be included in the ICF. Please note that In line with regulations/best practice future use of samples/personal data must be clearly explained to participants in the PIL/ICF so as to constitute broad informed consent, as required under the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018). Furthermore,

	- it should be confined to a specified disease, related diseases or drug under study in this trial. Consent can only be obtained where future use of samples and data is defined such that participants are fully informed, - and/or that an option is provided to enable participants to consent to be contacted in the future about other research studies, The PIL/ICF should also make it clear to participants that subsequent research ethics review will be sought for specific research once clearly defined. For further guidance, see: NREC guidance on use of biological samples and associated data - https://www.nrecoffice.ie/guidance-on-use-of-biological-samples-and-associated-data/ 4. Participant recruitment is to be performed by a suitably qualified member of the study team who is not involved in direct health care for the prospective participant to minimise the potential of any perceived coercion. 5. All participant facing documentation, including educational brochures which are mentioned in the application package, must be provided to the National Office prior to circulation to potential participants. 6. Clarification to be provided on which participants will receive a stipend of €60 for participating in the study.
10. 25-NREC-MD-015	• Principal Investigator (Lead Institution): Prof Damien Kenny and Prof Kevin Walsh (Mater Misericordiae University Hospital) • Sponsor: Medtronic Bakken Research Center • Study title: Harmony TPV EMEA Post-Market Study • NREC-MD decision: Request for further information • Further information requested: 1. While certain parts of the application were clearly laid out, the Committee request clarification on the study design. As this is a post-market study and the device was recently CE marked, the NREC-MD requires clarification on whether: - the device is routinely used in the study site and available to patients at the hospital outside of the study, - the device is considered standard of care in the study site, and - what other treatment options are available to prospective participants.

	2. The NREC-MD noted that participant consent may be obtained within 24 weeks prior to the implantation and request clarification for the delay between consent and procedure, and this timeline would be comparable for alternative procedures for this condition. 3. The NREC-MD noted that section K14 of the NREC-MD application form indicates that video will be collected and request clarification on the type of video recordings and their use in the clinical investigation. 4. The NREC-MD requests clarification on whether it is proposed that participants under 16 years of age are included in the clinical investigation. 5. The NREC-MD noted that prospective participants might have pre-existing clinical relationships with the research team/ PIs and request that clinical and research activities and teams are separated as much as possible to minimise any possibility of coercion. 6. The NREC-MD noted that the application refers to a "Patient brochure" however no such document was provided in the application dossier. The Committee request the role of the document is clarified and that a copy is provided for review. 7. The NREC-MD noted that Prof Damien Kenny is a consultant and proctor for the sponsor of the clinical investigation – Medtronic. The Committee noted that the PI is committed to the highest standard in research integrity, however given the conflict of interest, please outline what is the conflict-of-interest management plan for this study. 8. The NREC-MD noted that the PIL/ICF is overly technical and request that: - it is reviewed for accessibility and technical language, eg vital status checks. - the study lay title listed in the NREC-MD application form section A5 is included in the PIL/ICF, - the description of the procedure is revised for clarity, - the information on travel cost reimbursement is revised for clarity. 9. The NREC-MD requests that the PIL is revised to highlight that other treatment might be available for the participants. 10. The NREC-MD requests that the PIL is revised to include all study related procedures, e.g. additional testing etc. 11. The NREC-MD noted that the PIL states that "You have been invited to take part because of your heart issue" however this is inaccurate as participants have been invited as the clinical team

	identified them as potentially suitable for the implant and request the statement is revised. 12. The NREC-MD request the PIL is updated to include brief information on the device -how long has it been in use and how many participants have used the device so far and with what outcome. 13. All risks related with participation in this study must be listed and quantified in the PIL to facilitate informed consent. 14. The NREC-MD request the PIL/ICF is reviewed for compliance with the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), eg in relation to data transfer. 15. The NREC-MD noted that the future use of data/samples is not described consistently across the documentation. In line with regulations/best practice future use of samples/personal data must be sufficiently explained to participants in the PIL/ICF so as to constitute broad informed consent, as required under the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018). Furthermore, - it should be confined to a specified disease, related diseases or drug under study in this trial. Consent can only be obtained where future use of samples and data is defined such that participants are fully informed, - and/or that an option is provided to enable participants to consent to be contacted in the future about other research studies, The PIL/ICF should also make it clear to participants that subsequent research ethics review will be sought for specific research once clearly defined. For further guidance, see: NREC guidance on use of biological samples and associated data - https://www.nrecoffice.ie/guidance-on-use-of-biological-samples-and-associated-data/ 16. In relation to point 2 above, the PIL/ICF should highlight that video data will be collected and processed and that a separate consent form is provided for this.
11. 25-NREC-MD-016	• Principal Investigator (Lead Institution): Prof Damien Kenny (Children's Health Ireland - Crumlin) • Sponsor: Occlutech International AB • Study title: A multicenter, international, Prospective and Retrospective, post marketing clinical follow-up study to evaluate the efficacy and safety of the Occlutech Patent Ductus Arteriosus

	Occluder (The Occlutech PDA Occluder) in patients with Patent Ductus Arteriosus defects • NREC-MD decision: Unfavourable • NREC-MD Comments: 1. The Committee gave considerable time to review and discuss the application and noted the usefulness of the study. However, the NREC-MD noted that the application presented serious issues, in particular in the area of informed consent, and requires significant revision before it can be considered again by the Committee. 2. In its current form, the study documentation does not appear to meet requirements set out in Article 65 of the Medical Devices Regulations, in particularly in relation to paragraph (h) 'the minor shall take part in the informed consent procedure in a way adapted to his or her age and mental maturity'. 3. The aims and objectives of the study are not clearly set out in the application form. The Committee noted that the study objectives appear to be focused on gathering conformity data as well as on evaluation of the device compatibility and usability with other devices. However, information on these devices is not included in the application, e.g. are these additional devices CE marked, are they approved for use with the primary device. 4. It is not clear from the documentation which visits/examinations etc are standard of care and which are study specific. 5. There is no information about the procedures, processes and safeguards that are in place in the instance where a child is transferred to adult services while taking part in the study. 6. The Committee noted inconsistencies in the age groups described across different documentation, e.g. the application form section I3(a) states 'following age range:- children under 6 years- children from 6 to 9 years- teenager from 10 to 15 years', while the PILs and other documents reference children under 6 years old, children between 6 and 11 years old, children between 12 and 17 years old and adults. 7. The study includes participants who are under the age of 16 and so do not have the capacity to consent. However, the application form 'Section H – Participants Lacking Decision-Making Capacity' Page 19 is not correctly completed as the answer to question 'H1 Will all participants have the decision-making capacity to give informed consent?' is given as 'Yes' and no other information is supplied in the following relevant questions. 8. Section E6 of the NREC-MD Application form refers to a Statistical Analysis Plan that was not submitted.

	9. There are inconsistencies in the numbers of participants reported in the application form, e.g. section F2 mentioned 255 participants and section E1 states 205 participants. 10. In the NREC-MD Application form section I5, the applicant inappropriately responds 'no' to two questions: - 'I5 (a) is this study of such a nature that it can only be carried out on children.' - Application responded no. Given the age profile of the incidence of PDAs, this does not seem correct. - 'I5 (b) Does the study relates directly to a medical condition which minors have been diagnosed with.' - Applicant responded no. This is a study for children diagnosed with PDAs and so the answer is incorrect. 11. The study recruitment strategy is unclear. Application form section F5 states that participants will be identified by searching for devices used during Cath-lab procedures while section E4 states participants will be recruited before their procedure. 12. The application form question G5 is partially answered as it is lacking information on 'where and when informed consent will be obtained and how privacy will be ensured'. 13. The application does not demonstrate a clear and comprehensive understanding of how to recruit participants that are minors. 14. The applicants do not appear to be aware of the recent changes to consent for 16- and 17-year-olds. Please note: - Participant 16 years and older can consent to participation in a regulated study and consent to the processing of their data for the purpose of that study. - There is no requirement to seek consent from a Parents/Legal Guardian for the processing of personal data for participants aged 16 years and 17 years. - The statement in the application form section I4 'A participant reaching the age of 18 years old during the study will sign the adult consent form' is therefore incorrect. 15. Section F8 of the NREC-MD Application form states that person of any age can participant in the study from 3kg upwards and that 'subjects understanding the nature of the study and providing their informed consent to participation'. As this is a paediatric study, this inclusion criterion does not apply to all participants as Parents/Legal Guardian must be in agreement for a child less than 16 years to enrol.

	16. The application documents indicate inappropriate use of the words assent and consent. 17. The Patient Brochure is not in suitable language for children. 18. The Committee noted that the language and presentation of the study information in the PIL/ICF is not suitable nor appropriate for any of the groups to be able to give informed consent or assent. 19. The language of the PIL/assent forms for participants under the age of 6 years and between 6-11 years old are not readable or understandable for those age groups. The documents require simplification and should score in line with age grades for Flesch Reading Ease Score. 20. The PILs for under 6 years old, 6-11 year olds and 12-17 year olds contain the word 'quit' when referring to withdrawal. This has negative connotations. Other PILs use the word 'stop' and this is more appropriate. 21. The PIL for 6-11 year olds and 12-17 year olds contains concerning language e.g. 'No one will be angry with you and your doctor will continue to treat you, but with a different treatment', and 'You can always quit again. No one will be angry with you'. This is inappropriate and inadvertently lead to coercion to participate as a child may say 'yes' in fear that someone may be angry and if they don't take part, they will be different to other children. 22. The PILs for Adults and Parents/Legal Guardians contain overly technical and inaccessible language. For example, the section on interventions has been directly extracted from the CIP and it is not clear that the assessments are repeated over seven visits. This is unsuitable and requires simplification and explanation in plain and easy to understand language. 23. The PIL for Parent/Legal Guardians and the Adult PIL both contain untrue and concerning statements that would mislead and potentially frighten or pressure potential participants and/or Parents/Legal Guardians, specifically: 'The available alternatives are anticipatory medical care and open-heart surgery.' Page 7. There are other alternatives that are not open-heart surgery. It is unethical and wrong to state otherwise in participant-facing or other documents. 24. The PIL for Parents/Legal Guardians and the PIL for Adults both contain inappropriate language that could unduly pressure Parents/Legal Guardians or adult participant on the necessity to use the child's data, e.g. 'Also, authorizations to market medical devices and research involving people are ruled by strict and specific laws. The

	processing of your child´s data is necessary for the public interest in the field of public health, specially for post market studies and surveillance activities (device's safety and efficacy). The study Sponsor has a legal obligation to use your information to ensure your child´s safety and the integrity of the study result. The Sponsor needs this information to further develop the device and monitor its safety. This cannot be done without using information about your child (i.e., your information).' 25. Further to point 24, please note that consent is the legal basis for processing of personal data in health research such as this one. 26. The number of follow-up examinations is inconsistent in the PIL for Parents/Legal Guardians, e.g. Page 3 states that they will be asked to attend seven follow-up examinations and also states that they will be asked to attend 5 follow-up examinations. 27. Page 8 of the PIL for Parents/Legal Guardians incorrectly states that 'you have the right to request the deletion of all personal data of your child stored up to that point'. As this study is carried out under the Medical Device Regulations to record post-market safety and effectiveness of a device, collected data cannot be deleted as it is required for regulatory purposes. 28. It is not clear from the participant facing documents which examinations/visits/etc constitute the standard of care and which are additional study specific procedures. 29. The PILs should state that the participants are entitled to receive a copy of the aggregated study results, if they wish. 30. The PILs incorrectly describe study withdrawal in relation to the device e.g. PIL 12-17 year olds, Page 2 'However, it is important that an already implanted occluder can only be removed if medically necessary'. Withdrawal from the post-market study is not related to removal of the device but relates to the data that is collected as part of the study only. 31. The list of adverse events and risks in each participant facing document is not accompanied by the relevant likelihood and requires more information to explain them. 32. There is no reference to participant expenses or compensation in the participant facing documentation. 33. Overall, there is a lack of clarity of future uses as reflected in the DPO and DPIA documents. In line with regulations/best practice future use of samples/personal data must be sufficiently explained to participants in the PIL/ICF so as to constitute broad informed consent, as required under the Health Research Regulations

	(Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018). Furthermore, - it should be confined to a specified disease, related diseases or drug under study in this trial. Consent can only be obtained where future use of samples and data is defined such that participants are fully informed, - and/or that an option is provided to enable participants to consent to be contacted in the future about other research studies, The PIL/ICF should also make it clear to participants that subsequent research ethics review will be sought for specific research once clearly defined. For further guidance, see: NREC guidance on use of biological samples and associated data - https://www.nrecoffice.ie/guidance-on-use-of-biological-samples-and-associated-data/ 34. The consent lines for uses of the participant's data are not aligned with broad consent for future use and must be provided as an optional consent line so that participants can be enrolled in the study even if they do not consent for future use of their data. 35. As stated above, it is not clear from the documentation which visits/examinations etc are standard of care and which are over and above standard of care for the study. If it is the case that any are outside of the standard of care and for the study only, participants should be compensated for reasonable expense such as travel, meals etc. 36. The study insurance does not meet the requirements set out by the State Indemnity Guidance: Clinical Trials Health Research. 37. The budget document does not include figures for costs, and so the Committee cannot determine if there is appropriate funding available for the study. 38. The CTA document (Document 11) submitted as part of the application is incomplete and blank in many parts 39. There are inconsistencies in the timeframes for data retention across the submitted documentation. 40. In the submitted document 12b Page 11 section D, question 1, both 'yes' and 'no' are selected as an answer when the direction is to 'select one' 41. In the submitted document 12b, question F.1 noted that contractors / external parties may have access to personal data 'by mistake', which is not acceptable and should be corrected.

	42. The application form indicates that data will be transferred outside the EU for processing (section K2) however no separate consent line is provided for this. 43. The data journey is not clear from the documents. As the data will be stored in an EU database, it is unclear why the application documents refer to the USA in relation to data. 44. The answer given to application form section F7(b) is not relevant to the question and so the question is not answered.
12. 25-NREC-MD-017	• Principal Investigator (Lead Institution): Dr Andrew Simpkin (UHG) • Sponsor: UHG • Study title: A stagewise assessment of the ability of healthy volunteers to utilise pressure monitoring technology for improving the targeted application, monitoring, and maintenance of compression therapy • NREC-MD decision: Request for further information • Further information requested: 1. The NREC-MD notes that a number of sections from the NREC-MD application form were not completed e.g. Section K1, Q and R2(a). Review the NREC-MD application form and complete any outstanding sections / questions. 2. The NREC-MD application form states that participants of child-bearing potential are not included, however, participants aged 18-45 will be included in this study. Clarify this discrepancy. 3. The NREC-MD requests clarification on the exclusion criteria for this study as there are inconsistencies throughout the documentation. The criteria should also be expanded as they are currently too vague (e.g. leg issues and skin issues must be clearly defined and described). 4. The NREC-MD requests clarification as to whether participants will be informed or their results or not. If yes, clarify how and when this will occur. 5. The NREC-MD notes that participants will complete a short questionnaire to rate the comfort of the medical device, and that subjective feedback will be gathered on the overall experience and usability of the device. - Provide copies of any surveys or questionnaires used to collect this information. - Clarify how and when this information / feedback will be collected.

	6. The NREC-MD notes that Section K18 of the NREC-MD application form refers to the possible use of an external independent consultancy firm that specialises in biostatistical analysis in the analysis of study data. The NREC-MD requests the following information: - What company will be used? - Where is this company based? - Does the PI have any involvement with this company? If so, provide details. - Will any data be moved outside of the EU, if so what protections are in place? 7. The NREC-MD notes that while the Principal Investigator has excellent research experience and extensive experience in studies involving wound management, they are a statistician and not a healthcare professional. Clarify if any of the staff involved in this study are healthcare professionals and how they will be supporting the PI in their role. 8. The NREC-MD notes that trained staff will be present during session to assist and monitor safety and that first aid will be available for any unforeseen events. Are any of the staff healthcare professionals? Given the procedures involved, clarify what qualifications and training staff will have. 9. Given that the staff involved in this study do not appear to be healthcare professionals, clarify the following: - How will medical information be gathered from participants? - How will the study staff ensure that they have adequate knowledge to answer any medical related questions that participants have e.g. does a specific skin disorder fall under the exclusion criteria of “skin issues”. 10. The NREC-MD requests confirmation that participants will be given a minimum of 24 hours to consider their participation in the study. 11. In order to fully understand the study, the NREC-MD requests further information on recruitment processes. Provide information on: - How potential participants will be identified - Who will first approach the potential participants - How will the first approach to the potential participants be conducted - How will the sponsor ensure that potential participants do not feel compelled to participate

	12. The NREC-MD notes that there are inconsistencies in how recruitment processes are described (e.g. the use of local advertisement in the NREC-MD application form vs the documentation checklist). Clarify this discrepancy. If local advertisement, posters or participant facing documents are to be used for recruitment purposes, these should be provided for committee review. 13. The NREC-MD notes (page 16 of the NREC-MD application form) that an initial screening process will be used prior to recruitment of participants. Clarify how this will be done and who will be involved in this process. 14. The PIL/ICF should be updated to include more information on the guided exercises and activities involved in the study. 15. The NREC-MD request the PIL/ICF is reviewed for compliance with the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018). For example, the PIL/ICF should be updated to include - more information on the legislative basis of data processing, - what happens to participant data if a participant withdraws from the study - where data will be stored and for how long - who will have access to participant data - the consent form is revised to provide unbundled consent, ie separate boxes are included for all consent statements in the ICF. 16. Clarify whether the Principal Investigator will be provided with any additional fees/ payments for the conduct of the study. If the PI will be provided with additional payments, provide a copy of the financial disclosure form. 17. The NREC-MD are concerned about the lack of insurance for this study. Review the State Indemnity Guidance: Clinical Trials Health Research and provide a stronger justification for proposed approach of no study specific insurance. Clarify what would happen if a participant developed skin issues or other during the study and who would bear the cost of their care or of a compensation for injury. 18. The NREC-MD notes that University of Galway is the sponsor and that Feeltech have been put down in error. However, it appears that Feeltech Ltd will be involved in the data processing / funding of this study. Clarify exactly what role Feeltech will play in this study and how much involvement they will have in the study e.g. data processing, financing etc.

13. 25-NREC-MD-018	• Principal Investigator (Lead Institution): Dr Fergal Donnellan (St Vincents Hospital) • Sponsor: St Vincents Hospital • Study title: Introducing an optical sensor capsule to the emergency department to detect upper GI bleeding • NREC-MD decision: Request for further information • Further information requested: 1. The NREC-MD requests clarification if due consideration has been given to Article 68 of the Medical Devices Regulation (clinical investigations in emergency situations). Clarify whether it may apply to the proposed study. 2. The NREC-MD request clarification on whether the study has been assessed by the Health Products Regulatory Authority and if so, provide details. If not, the Committee strongly recommend that they are engaged with prior to submitting a Request For Further Information response. 3. Given that patients in emergency situations will be recruited for this study, Section F11 of the application form must be completed. 4. The NREC-MD requests that the PI card is updated to include contact details for the participant to use should any adverse event occur. 5. The NREC-MD notes that the clinical investigation plan (CIP) requires a substantial revision to comply with the requirements set out in Annex XV of the Medical Device Regulation and must be updated to address the following: - Clearly state what the study aims are - Clearly state what the endpoints of the study are - Clarify exactly how the study design will fulfil the aims of the study e.g. how will it be demonstrated that the PillSense system is more sensitive and specific than the Glasgow Blatchford Score (GBS). - Section 5.1 along with other sections of the CIP appear to be missing and must be included in the document. 6. The NREC-MD notes that the CIP currently indicates that the study aims to evaluate safety and effectiveness of the device in suspected non-variceal upper GI bleeds, however, it is not clear how the inclusion/exclusion criteria would identify and exclude

	suspected variceal bleeds. If suspected variceal bleeds are excluded, these must be listed in the criteria. 7. The NREC-MD notes that the data collection form includes two additional exclusion criteria not listed in the CIP or PIL/ICF; 'patients with known upper GI pathology or recent relevant procedures' and 'patients with altered mental status'. Clarify this discrepancy update the documentation accordingly. 8. The NREC-MD requests clarification as to whether patients with swallowing difficulties will be recruited for this study. 9. The NREC-MD requests clarification as to whether only patients with a GBS indicating suspected GI bleed, or those where emergency endoscopy is planned, will be subject to the intervention, or if all suspected GI bleed patients will be considered for enrolment in this study. 10. The NREC-MD notes that pregnant participants will be excluded and a pregnancy test will be used to determine this. However, give the risk of false negatives with pregnancy tests, especially in early pregnancy, and the necessity of imaging should the device be retained, the NREC-MD requests that participants who think there is a chance they are pregnant are excluded from this study. 11. The NREC-MD notes that Section 2.3 of the CIP states that the PillSense device is prescription only. Clarify how this will be documented on a patients chart so that the clinical team are aware of the participant being enrolled in the study. 12. While the NREC-MD notes that the PillSense capsule will be excreted naturally, it is currently unclear how this will be monitored and what form of disposal is required. The NREC-MD requests more information on the post use handling and recommended method of disposal of the device for participants. Given that the device contains a battery, information on relevant safety or environmental considerations should also be included in the response. This should be included in the CIP and participant information leaflet/ informed consent form (PIL/ICF). 13. The NREC-MD notes that a potential x-ray may be required should the capsule not be excreted within the relevant time frame. Therefore, Section O of the application form must be completed and this information must be included in the PIL/ICF. 14. The NREC-MD request clarification on what happens when the PillSense results show no blood is present. Will the participants still undergo endoscopy as per standard of care if a bleed is suspected by their clinician? 15. Section F20 of the application form must be completed.

	16. Section G9 of the application form suggests that consent withdrawal management will depend on which category of treatment the patient falls under. Given that there is no control group and all participants will have ingested the device, this section should be revised for clarity. 17. Given the nature of this study, the NREC-MD requests that the participant's GP be informed about their involvement with this study. A copy of the GP letter template must be provided for review. 18. The NREC-MD requests clarification on how safety events will be monitored, assessed and reported. If the study involves a Data Safety Monitoring Committee, proposed membership and terms of reference must be included in the response. 19. The NREC-MD requests clear justification for the sample size of 30 participants. This should be included in the CIP. 20. The NREC-MD notes that the participant group is limited to adults over 18 years old with capacity to consent. Given that participants aged 16 and older can consent to participate in clinical research as per the HSE National Policy for Consent in Health and Social Care Research, the NREC-MD requests justification for the proposed age limit. 21. The NREC-MD notes that recruitment is being done via standard triage in an emergency department setting. Clarify whether out of hours recruitment will occur and how this will be done. 22. Clarify who will be approaching prospective participants in relation to their participation in the study and whether there will be any overlap between research and clinical team. If not, outline how will it will be ensured that any potential for perceived coercion is minimised. 23. The NREC-MD notes that potential participants will be given a 30-minute window to decide whether or not they wish to participate in this study. Provide a strong and thoughtful justification as to: - why this time window was chosen, - how it fits in within standard ER triage and treatment times, - how it is preferable to other possible longer timeframes and finally - how will it be ensured that prospective participants are truly in a position to provide informed consent for their participation. 24. The NREC-MD notes that those with a contraindication to ingestible capsules (e.g. IBS or previous GI surgery) will not be considered for this study. However, given that the recruitment

Commented [LH1]: Falls under HPRA remit so may not need to include

	window is quite narrow, clarify how the study team will ensure that potential participants do not meet any of the exclusion criteria (e.g. in out of hours situations, without GP input etc). 25. The PIL/ICF in its current format is not fit for purpose and should be extensively revised to improve readability and accessibility. The below is a non-exhaustive list of points to include in the PIL/ICF: - A brief and descriptive title of the study - A background to the study and why it is being conducted, including clear aims - A detailed description of the study device and how it pertains to the study - A detailed description of all study related procedures and follow up required by potential participants - A list of all the benefits and risks - The risk of sensor retention should be elaborated to include the likelihood of this occurring and the course of action to resolve this should it occur (e.g. surgical intervention). - A clear statement that participation is voluntary and participants can withdraw at any time. A description of what happens to the participants data should they withdraw should also be included - Information on what data will be collected and stored, how it will be stored and who will have access to it - Concerning language such as “a clear message will be delivered to your physician on whether blood is present or not requiring no interpretation from your clinical team” should be removed. Given that this is an investigational medical device and in fact all medical investigations ultimately need interpretation from the clinical team, this statement is inappropriate. 26. Section K1 of the application form should be revised to account for all data processed during screening, recruitment, consenting, and during procedures. 27. Section K7 of the application form states that data will be anonymised at the end of the study. The NREC-MD requests confirmation on when this will be (e.g. end of recruitment, post data analysis etc). 28. Section K16 of the application form should be revised. As data will be pseudonymised, it will be possible to reidentify participants.

	29. Section K18, K22 and K23 of the application form should be revised. 30. The NREC-MD notes that this study does not appear to be funded or have any funding. Clarify or provide a strong and detailed justification for this. In particular, clarify who will bear the cost of recruitment, monitoring and follow up of participants, e.g. should the device need to be surgically removed.
14. 24-NREC-MD-020-SM1	• Principal Investigator (Lead Institution): Prof. Ronan Cahill (Mater Private Network) • Sponsor: UCD • Study title: CLASSICA: Validating AI in Classifying Cancer in Real-Time Surgery • NREC-MD decision: Favourable
15. 24-NREC-MD-025-SM1	• Principal Investigator (Lead Institution): Prof Fergal Malone (Rotunda Hospital) • Sponsor: BillionToOne • Study title: Fetal Antigen NIPT Clinical Trial Assay (CIV-23-09-043953) for use in Janssen-Cilag International NV IMP Study 80202135EBF3001 • NREC-MD decision: Favourable
16. AOB	• Two new NREC-MD application forms (one for Medical Device Regulation and one for In Vitro Medical Device Regulation) will be rolled out over the coming months. • A new statement of compliance form has been published on the National Office website. The previous version will be phased out over the coming months.