# National Research Ethics Committee

## NREC-CT B Meeting

**23 November 2022**

### Attendance

| Name | Role |
|---|---|
| Dr Cliona McGovern | Chairperson, NREC-CT B |
| Dr Jean Saunders** | Deputy Chairperson, NREC CT-B |
| Prof. John Faul | Deputy Chairperson, NREC-CT B |
| Ms Serena Bennett | Committee Member, NREC-CT B |
| Mr Philip Berman | Committee Member, NREC-CT B |
| Dr Enda Dooley | Committee Member, NREC-CT B |
| Dr Lorna Fanning | Committee Member, NREC-CT B |
| Dr John Hayden | Committee Member, NREC-CT B |
| Dr Mary McDonnell Naughton | Committee Member, NREC-CT B |
| Dr Eimear McGlinchey | Committee Member, NREC-CT B |
| Mr Gavin Lawler, | Committee Member, NREC-CT B |
| Ms Paula Prendeville | Committee Member, NREC-CT B |
| Prof. Colm O'Donnell | Committee Member, NREC-CT B |
| Ms Caoimhe Gleeson | Committee Member, NREC-CT B |
| Prof. Abhay Pandit | Committee Member, NREC-CT B |
| Dr Mark Robinson | Committee Member, NREC-CT B |
| Ms Mandy Daly | Committee Member, NREC-CT B |
| Prof David Smith | Committee Member, NREC-CT B |
| Prof Andrew Green | Committee Member, NREC-CT B |
| Ms Susan Kelly | Committee Member, NREC-CT B |

| | |
|---|---|
| Ms Deirdre MacLoughlin | Committee Member, NREC-CT B |
| Prof Seamus O'Reilly | Committee Member, NREC-CT B |
| Dr Christina Skourou | Committee Member, NREC-CT B |
| Dr Emily Vereker | Acting Head, National Office for RECs |
| Dr Jane Bryant | Project Officer, National Office for RECs |
| Dr Susan Quinn | Programme Officer, National Office for RECs |
| Dr Emma Heffernan* | Project Officer, National Office for RECs |

*Drafted minutes

** Meeting Chair

**Apologies:** Ms Mandy Daly, Prof. Colm O'Donnell

**Quorum for decisions:**

Yes

## Agenda

- Welcome & Apologies
- 22-NREC-CT-171
- 22-NREC-CT-172
- 22-NREC-CT-173
- 22-NREC-CT-174
- 2022-501352-28-00
- 2022-501238-52-00
- AOB

---

- The Chair welcomed the NREC-CT B.
  - The minutes from the previous NREC-CT B meeting on 19 October 2022 were approved.
  - The NREC Business Report was discussed and noted.

## Applications

**22-NREC-CT-171**

Principal Investigator:

Study title: Safety and efficacy of inhaled pegylated adrenomedullin (PEG-ADM) in patients suffering from Acute Respiratory Distress Syndrome (ARDS): a double-blind, randomized, placebo-controlled, multicenter Phase 2a/b clinical trial (SEAL)

EudraCT: 2020-002324-36

Lead institution: St Vincent's University Hospital

- **NREC-CT comments:**

The NREC-CT B agreed that additional information was required to inform its deliberations before a final ethics position could be returned.

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

- The NREC-CT noted a number of typos and inconsistencies across the NREC Application Form and requested that all documents are thoroughly proof-read for accuracy.
- The NREC-CT requested clarity regarding consenting of participants onto the trial, who lack decision-making capacity. The Committee noted that the amendment (S.I. No. 18 of 2021) to the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations) in 2021 provides for participants who lacks decision-making capacity to be enrolled in a study in the absence of consent, if the study is in the vital interest of the person. Note, a legal representative cannot lawfully consent for the processing of personal data for health research, on behalf of a participant who lacks decision-making capacity to consent.
    - The applicants must specify whether they are relying on this amendment. If not, it will be necessary to apply for a consent declaration from the HRCDC to ensure compliance with the Regulations.
    - Secondly, please comment on and how and when deferred consent will be obtained from the participant once decision-making capacity is regained.
    - The NREC-CT requested that reference to the Health Research Regulations 2018, and if relevant, to the Health Research Consent Declaration Committee, is set out in PISCF documents.
    - Where participants do not regain decision-making capacity, please outline what will happen to the processing of personal data and collection of biological samples.

- The NREC-CT noted that minimal interval of 6 hours between doses suggests there may be side effects if doses are given in a closer timeframe. The Committee requested that the applicants consider documenting the risk of overdose and mitigation for same.
- The NREC-CT recommended that the PISCF should be adapted for Irish participants, who will only participate in Part B of the study. The Committee recommended that details of Part A including randomisation be removed/summarised and the schedule of activities could be separated out for the participants.
- The NREC-CT requested the following regarding future use of samples/data:
    - i) that consent for future use of samples is provided on a separate consent form and not bundled,
    - ii) is made optional,
    - iii) confirmation is provided that subsequent research ethics review will be sought for specific research once clearly defined
- The NREC-CT requested clarification is provided regarding the reason for provision of a tracked changes version of PIL/ICF for review
- The NREC-CT recommended the applicants consider whether language in the relative assent form could be more sensitive, considering their relative may be acutely unwell
- The NREC-CT requested that reference to the Ethics Committee is removed from the sentence: “I understand that apart from the study doctor and study staff, a small group of people working on behalf of the sponsor, <<Ethics Committees/Institutional Review Board> and regulatory authorities> may need to see my un-coded personal information”
- The NREC-CT A requested that the applicant provides additional information in Section 4-7 on the facilities available at the SVUH site to support this study.
- The NREC- noted that the study insurance certificate provided does not cover the whole trial duration and requests assurance that the trial will be adequately insured for the whole duration and will cover all sites

**22-NREC-CT-172**

Principal Investigator: Dr Grainne O'Kane

Study title: A Phase 1b/2a Dose Escalation Study of BOLD-100 in Combination with FOLFOX Chemotherapy Patients with Advanced Solid Tumours

EudraCT: 2022-003079-41

Lead institution: St James’s Hospital

- **NREC-CT comments:**

The NREC-CT B agreed that additional information was required to inform its deliberations before a final ethics position could be returned.

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

- The NREC-CT requested further detail is provided on screening and recruitment, including the number of participants to be screened, and how recruitment will take place.
- The NREC-CT commended the applicants on provision of a summary Participant Information Leaflet. The Committee noted that the document should include the risks of participation in the study, and that the applicants may wish to consider this guidance issued by the National Office.
- The NREC-CT suggested that the participant materials would benefit from the addition of graphs/visuals to aid accessibility.
- The NREC-CT noted that it is stated that each visit will take 48-50 hours (page 3, main PISCF). Please clarify if this is an error.
- The NREC-CT noted that the 'What do you need to do?' section needs more detail. Please clarify in the PIL what the biomarker analysis involves and provide justifications for the clinical examinations and blood samples being collected. The PIL should also clearly define what genetic analysis is being done as part of the biomarker analysis.
- The NREC-CT noted that Inclusion and Exclusion criteria are missing from Appendix A.
- The NREC-CT noted that the consent material layout is not in line with best practice and requests that the applicant provides participants with a layered approach to consent.
- The NREC-CT noted that the PIL/ICF is seeking blanket consent for future use of samples / data, for unspecified purposes, without further consent ("*I agree that my leftover samples that were already collected for this study may be used for future research studies that are unknown at this time"*). This type of consent not in line with best practice, the Declaration of Taipei 2016 and not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), where informed participant consent is a mandatory safeguard. The NREC-CT requests:
    - that consent for future use of samples is provided on a separate consent form and not bundled
    - is made optional, and
    - 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 is provided in a separate consent form.
- The NREC-CT noted that an impartial witness or translator is included for both literacy and language issues. The Committee requested that the PIL should include a statement to clarify that the translator and/or impartial witness is not consenting on the participant's behalf, and that signed participant consent is still required.

- The NREC-CT requested rewording of aspects of the PIL/ICF to ensure it is accessible to all participants. The Committee deemed there are messages which the participant may find confusing, and requested edits as below:
    - Regarding approval of the use of the drug (page 2, PIL/ICF) “health authorities have not approved the use of bold 100 for any type of cancer but have allowed its use in this study”. Please provide further information to the participant, including details of the Health Authority.
    - Please include an explanation as to what sharing of “coded” data means for participants.
    - Please provide further explanation as to what “Tested safety in animals” means for participants.
    - The noted side effects include anorexia, please provide further context/explanation for participants.
- The NREC-CT requested that the text on travel and expenses is adapted to provide clarity on what will be covered in Ireland, and what is the maximum amount of compensation provided to participants for travel and refreshments and that this be further elucidated in the PIL.

**22-NREC-CT-173**

Principal Investigator: Prof Bryan Hennessy

Study title: Single arm phase 2 trial of neoadjuvant trastuzumab deruxtecan (T-DXd) with response-directed definitive therapy in early stage HER2-positive breast cancer: a standard chemotherapy-sparing approach to curative-intent treatment – SHAMROCK study.

EudraCT: 2022-002485-32

Lead institution: Beaumont Hospital

- **NREC-CT comments:**

The NREC-CT B agreed that additional information was required to inform its deliberations before a final ethics position could be returned.

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

- The NREC-CT noted that pg. 19 of the PIL suggests that the wash out period for T-DXd is 4 months and requested clarification as to how quickly a participant that shows disease progression can be moved to Standard of Care treatment

- The NREC-CT requested that the additional risk from the required multiple mammograms is described in lay terms in the PIL
- The NREC-CT consider the PIL to be excessively long, complex and repetitive in places and requested that the PIL is revised and that a trial summary is made available for participants The NREC noted that the first two pages of the PIL could be a basis for this summary, and that the applicants may wish to consider this guidance issued by the National Office.
- The NREC-CT requested that an explanation for the following terms is provided for participants in the PIL – regimen, gut microbiome, RDI score, pulse oximeter, SpO2.
- The NREC-CT noted that pg. 12 of the PIL states that "Insertion of radio-opaque clip to mark the tumour […] needs to be made in women…". The NREC-CT requested clarification if the same procedure is required for men with breast cancer and if so, that this is added to the PIL.
- Furthermore, the NREC-CT requested that all documentation is reviewed to ensure wherever "women" are addressed, the same is done for men, as the trial is open to both men and women
- The NREC-CT noted that pg. 14 of the PIL states that: "after the end of study treatment […] your doctor will decide if you will have additional treatment after surgery…" and requested clarification whether participants will be reconsented for the additional weeks on the drug post-surgery - if not, the current PIL must have an explicit line regarding the additional time.
- The NREC-CT noted several references in the PIL for future use of samples / data, for unspecified purposes, without further consent. This type of consent not in line with best practice, the Declaration of Taipei 2016 and not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), where informed participant consent is a mandatory safeguard. The NREC-CT requests:
    - i) that consent for future use of samples is provided on a separate consent form and not bundled,
    - ii) is made optional, and
    - iii) consent can only be obtained where future use of samples and data is defined such that participants are fully informed, and/or
    - iv) that an option is provided to enable participants to consent to be contacted is provided in a separate consent form.
    - The NREC request confirmation that subsequent research ethics review will be sought for specific research once clearly defined
- The NREC-CT noted that participants will not be reimbursed for trial participation. The NREC-CT requested that to ensure equitable access to clinical trials across all socio-economic groups that trial participants are reimbursed for reasonable out-of-pocket expenses. The NREC-CT requested the following:
    - A detailed description of the trial related expenses participants are permitted to claim (such as travel, parking, refreshments, etc) is provide in

the PIL, so participants are reassured that trial participation will not leave them out-of-pocket

  - Details on the process involved in claiming expenses and how and when they will be reimbursed.
  - Additionally, the NREC-CT requests that a participant should be permitted to bring a companion for these visits, and that this companion should also be eligible for reimbursement.

- The NREC-CT noted that the study insurance certificate provided does not cover the whole trial duration and requests assurance that the trial will be adequately insured for the whole duration and will cover all sites.

-

**22-NREC-CT-174**

Principal Investigator: Dr Patrick Thornton

Study title: A Phase 2 Study to Evaluate the Efficacy and Safety of MK-1026 in Participants with Hematologic Malignancies

EudraCT: 2020-002324-36

Lead institution: Beaumont Hospital

- **NREC-CT comments:**

The NREC-CT B agreed that additional information was required to inform its deliberations before a final ethics position could be returned.

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

- The NREC-CT requested clarification as to the length of the trial in Ireland and the length of the global trial.
- The NREC-CT noted that document 15 describes details of drug continuation beyond disease progression and requested that this is also detailed in the protocol.
- The NREC-CT requested that the GP letter includes reference to the use of the trial drug as being experimental.
- The NREC-CT A noted in the inclusion of a QoL questionnaire and requested that should this questionnaire indicate a mental health issue, details as to the pathway of care and referral offered to participants are elucidated in the PISCF.
- The NREC-CT noted that documents 11 and 13 outline that in future biological research, results will not be made available to participants. The NREC-CT requested justification

regarding this lack of information in the event that a germline mutation be discovered which e.g., increases the risk of cancer.

- The NREC-CT noted that pg. 12 of the Application Form states, *'all reported pregnancies will be followed to the completion/termination of the pregnancy'* and requested that this is also added to the PISCF.
- The NREC-CT noted that Pg. 9 of the Application Form that states that during screening *"A sample of another tissue can be given …"* and requested clarification as to the nature of this tissue sample and the procedure required to obtain it.
- The NREC-CT noted that the advice given to participants re fasting before and after taking the trial drug differs in the PISCF, the diary and the Application Form and requested that this is aligned across all trial documentation.
- The NREC-CT commended the applicants on provision of a summary Participant Information Leaflet. However, the Committee consider that the document was too brief and should include detail of the number of study visits. The applicants may wish to consider this guidance issued by the National Office.
- The NREC-CT noted that it is not clear as to the nature and number of visits required and requested that a clear estimate of the number of visits, the nature of visits and the projected length of time of each visit, over the course of the study is elucidated in the PISCF
- In line with best practice the NREC-CT requested that the Addendum to the Consent Form for Treatment after Disease Progression includes a layered approach to consent.
- The NREC-CT also noted that participants should be advised to bring a snack / light refreshments with them to trial visits, as the trial visits are potentially long and require participants to fast.
- The NREC-CT requested that the pregnant partner PISCF is submitted for review
- The NREC-CT requested that the following sentence on pg. 14 of the PISCF is reworded "*This research is exploratory and is not meant to provide any information that is useful to you or your doctor*."
- The NREC-CT requested that the SSA for University Hospital Limerick is fully completed and details the suitability of the facilities and equipment available.
- The NREC-CT requested a more detailed CV is provided for Dr Thornton, detailing previous clinical trial experience and evidence of up-to-date ICH-GCP certification**.**
- The NREC-CT noted that there is conflicting information in the Application Form (pg.28) and the FBR PISCF regarding the length of time biomaterial will be retained for and requested that the length of time that biomaterial is retained for is clarified, and this is aligned across all relevant documentation.
- The NREC-CT requested that both the FBR and Optional Biopsy Sample consent forms confirm that agreements are in place so that in the event of transfer of data outside EU, equivalent GDPR protections will apply.
- The NREC-CT noted that the DPIA describes the initial likelihood of a cybersecurity threat as 'limited' and recommended that this is adjusted, considering the recent cybersecurity attacks on Irish health care organisations/ providers.

- The NREC-CT deemed that there is a discrepancy in how reimbursement is outlined in the Application Form and the PISCF and requested clarification as to the reimbursement arrangements for participants and this is explained in the PISCF
- The NREC-CT queried whether an overnight stay will be required. If an overnight stay is required, the NREC-CT requested that details are explained in the PISCF.

**2022-501352-28-00**

Principal Investigator: N/A

Study title: A randomized, placebo-controlled, double-blind, multi-center, phase III trial to assess the efficacy and safety of trimodulin (BT588) in adult hospitalized subjects with severe community-acquired pneumonia (sCAP)

EudraCT: 2022-501352-28-00

Lead institution: N/A

- **NREC-CT comments:**

The NREC-CT B agreed that additional information was required to inform its deliberations before a final ethics position could be returned.

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

- The NREC-CT requests that specific detail is provided as to how all emergency consent procedures undertaken in comply with all parts of Article 35 of S.I. No. 40/2022 – European Union (Clinical Trials on Medicinal Products for Human Use) Regulations 2022.
- The NREC-CT requests information on informed consent supports available to participants who do not lack capacity to consent, but who may still be in an emergency situation
- The NREC-CT requests notes weight-based dosing is used, and BMI over 40 is an exclusion criteria. The NREC-CT requests further information on whether dose capping at any limit should apply for participants at extremes of weight.

- The NREC-CT notes a Covid-19 diagnosis within the previous four weeks is an exclusion criteria, number 6. The NREC-CT requests further information on whether this includes Covid-19 like symptoms without a positive PCR test, similarly for a positive antigen test without a PCR test.

- The NREC-CT requests information on whether those with a potential healthcare-associated pneumonia (i.e. coming from a community residential facility like a nursing home, and not a hospital or home environment) are eligible for inclusion.
- The NREC-CT notes that Fluroquinolones are not permitted due to the risk of drug interactions, and requests clarification whether for beta-lactam allergic patients, there is protocol guidance for selecting permitted alternatives, mindful of different national guidelines, and local Cultures and Sensitivities. The NREC-CT notes this may reduce risk of a perceived lack of treatment options during out of hours recruitment and treatment.
- The NREC-CT notes that the submitted Clinical Frailty Score mentions 'scoring frailty in people with dementia' and requests clarification on whether this will be used for all participants, regardless of their dementia status.

**2022-501238-52-00**

Principal Investigator: Prof. Colin McMahon

Study title: A Phase 2/3 Randomized, Placebo-Controlled, Double-blind, Clinical Studyto Evaluate the Efficacy, Safety, and Pharmacokinetics of Vericiguat in Pediatric Participants with Heart Failure due to Systemic Left Ventricular Systolic Dysfunction (VALOR)

EudraCT: 2022-501238-52-00

Lead institution: CHI Crumlin

- **NREC-CT comments:**

The NREC-CT B agreed that additional information was required to inform its deliberations before a final ethics position could be returned.

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

- The NREC-CT notes that the minimum volume of blood proposed to be taken in children 28 days to 2 years is 13 ml, in addition to clinical indicated blood samples. In a 1-month-old baby, that is the equivalent of 600ml from an adult. The NREC-CT deemed this excessive, and request that these volumes needed to be reviewed. The NREC-CT recommends consulting the EU guidance on children and clinical trials for recommendations on blood volumes.

- The NREC-CT notes that each visit may take up to 6 hours, and requested further detail on provision of subsistence and parking availability or reimbursement.
- The NREC-CT notes in the Main ICF, that if the participant has not consented for the study team to contact their GP or view their medical records, or in the event that that the study team cannot contact the participant, that publicly available sources can be used to find contact information. The NREC-CT recommends that if the participant has not consented to this contact, that this should be respected
- The NREC-CT notes that it is stated in the FBR Assent Form for 6–9-year-old participants, that a company called MSD is paying the hospital to do the FBR. The NREC-CT requests that this be clarified and communicated in the Assent Form, including to determine where the FBR samples are obtained, where the samples will be analysed, and who has responsibility for performing the FBR.
- The NREC-CT notes that the Participant Identification Number and the participant's name are present on the ICF documents, and requests confirmation that this will not compromise the participants' identity
- The NREC-CT requests clarification on whether participants who reach 18 will be reconsented for FBR, if their parents have previously provided consent for same
- The NREC-CT requests further detail on Dr McMahon's clinical research experience, if available.

---

- AOB: