National Research Ethics Committee

NREC-CT Meeting

27th August 2025

Attendance

Name	Role
Dr John Hayden	Deputy Chairperson, NREC CT-B
Prof Colm O'Donnell	Deputy Chairperson, NREC-CT B
Ms Serena Bennett	Committee Member, NREC-CT B
Dr Åine de Róiste	Committee Member, NREC-CT B
Dr Karina Halley	Committee Member, NREC-CT B
Prof. Michaela Higgins	Committee Member, NREC-CT B
Dr Ciaran Lee	Committee Member, NREC-CT B
Dr Andrew Lindsay	Committee Member, NREC-CT B
Ms Evelyn O'Shea	Committee Member, NREC-CT B
Mr Ed McDonald	Committee Member, NREC-CT B
Ms Chita Murray	Programme Manager, National Office for RECs
Dr Jane Bryant	Project Officer, National Office for RECs
Dr Laura Mackey	Programme Officer, National Office for RECs
Dr Susan Quinn	Programme Manager, National Office for RECs
Dr Peadar Rooney	Project Officer, National Office for RECs

Apologies: Dr Cliona McGovern, Prof Seamus O'Reilly, Dr Niall McGuinness, Ms Ann Twomey, Ms Jasmine Joseph

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2024-518926-34-00
- 2024-518365-10-00
- 2025-522216-17-00
- 2025-521697-34-00
- 2024-516030-35-00 SM-3
- 2024-514173-22-00 SM-6
- 2023-504807-94-00 SM-10
- 2024-511754-41-00 SM-4
- AOB

- The Chair welcomed the NREC-CT B.
  - The minutes from the previous NREC-CT B meeting on 2nd July 2025 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2024-518926-34-00

Institutions: N/A

Study title: A Phase 3, Randomized, Open-Label study of BET-Inhibitor INCB057643 Versus Best Available Therapy, in Participants with Myelofibrosis Previously Treated with a JAK Inhibitor (BET-MF2)

Dossiers Submitted: Part I

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part I Considerations (RFI) for addition to CTIS

- It was noted that the FDA requested further justification for not enrolling patients with baseline platelet threshold of ≥150,000, as per the ongoing phase 1

monotherapy study (pg. 7 Scientific Advice Summary FDA). Please justify the platelet cut off of ≥ 100,000 (Protocol pg. 49) given the risk of bleeding.

- It was noted that a long-term plan for monitoring malignancy was recommended by the FDA (pg 11 Scientific Advice Summary FDA) but sufficient detail has not been included in the Protocol (Protocol pg. 97). Please ensure that a detailed long-term plan for monitoring malignancy is included in the protocol.

- It was noted that very limited preliminary efficacy and safety data in patients with myelofibrosis from the associated Phase 1 trial, Study INCB 57643-103, was provided (pg. 6 Scientific Advice Summary FDA). Please provide further efficacy and safety data to support the proposed Phase 3 protocol.

- It was noted that the FDA did not agree that the proposed study population of patients who have received at least 1 prior JAK inhibitor therapy to be sufficiently refractory or intolerant to all available FDA approved therapies (Scientific Advice Summary FDA). Please justify your definition of refractory and intolerance to JAK inhibitor treatment and provide rationale as to why patients would not benefit from an alternate JAK inhibitor after failure of one prior JAK inhibitor based on their clinical manifestations and type and severity of anaemia.

2024-518365-10-00

Institutions: St James's Hospital, Mater Misericordiae University Hospital, Tallaght University Hospital, Beaumont Hospital

Study title: A Phase III, Randomized, Open-Label Study Evaluating The Efficacy and Safety of Divarasib and Pembrolizumab Versus Pembrolizumab and Pemetrexed and Carboplatin or Cisplatin in Patients with Previously Untreated, KRAS G12C-Mutated, Advanced or Metastatic Non-Squamous Non-Small Cell Lung Cancer

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations

1. Financial arrangements

- The NREC-CT noted that reimbursement for participants' meals and accommodation is listed in the Compensation for Participants Form (pg1) but is absent from the Main ICF (pg7). The NREC-CT request that reimbursement for participants accommodation and meals is also listed in the Main ICF.

- The NREC-CT noted that carers of participants have not been included for travel, accommodation and meal expense reimbursement in the Compensation Form (p1). The Committee requested that reimbursement of travel, accommodation and meal expenses are considered for carers of participants and, if included, that it is elucidated in the Compensation Form and PISCF's.

2. Subject information and informed consent form

- If applicable, the Sponsor is requested to submit any Part 2 documentation that require updates as a result of the Part 1 Assessment. Please include detail of the Part 1 consideration that triggered the update to the Part 2 documentation.
- The National Office requests that all documentation provided in response to RFI is presented in an accessible and searchable format (Word or original PDF). We are unable to accept scanned documents (including documents modified using Optical Character Recognition) as these documents cannot be optimised for use with assistive software.
- The NREC-CT noted the sentence 'You will undergo a biopsy at the time of disease progression' (pg 38 Main ICF). The Committee requested that the sentence is amended to clarify that the biopsy is optional.
- The NREC-CT noted that participants consent to their General Practitioner (GP) being contacted about study participation and related medical information (pg 35). The NREC-CT request that the submission of a GP Letter for review.
- The NREC-CT noted the sentence 'I will be given a copy of all 52 pages of this form after it has been signed and dated' (Main ICF pg 36) and observed that that this may be confusing for the participant as Section 3 and 4 of the Main ICF are optional. The Committee request that the above sentence is amended to reflect that only relevant/applicable sections are required to be signed and dated.
- The NREC-CT noted that consent questions regarding data protection (Main ICF pg 45) are separated from the other consent questions relating to Section 4. Furthermore, the NREC-CT noted a typographical error at the end of Section 4 (pg 45) which incorrectly requests the patient to confirm that they have "read this section 3 in full". The Committee requested that consent sections relating to Section 4 are merged if applicable and that the typographical error is amended to ensure informed consent.
- The NREC-CT noted that participants will be required to complete questionnaires relating to their health status and symptoms (pg 28). The Committee request that the time burden of the questionnaires be elucidated in the ICF and whether the questionnaire will be digital or paper based be specified.
- The NREC-CT noted that the future use of data / samples (including genetic research) is not described in line with regulations / best practice on pg. 41 of the Main ICF or pg. 4 of the Compliance of Biological Samples Form. The NREC-CT requested that future use of samples / personal data is sufficiently explained to participants in the ICF documents 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 PISCF should also make it clear to participants that subsequent research ethics review will be sought for specific research once clearly defined. For further guidance, please see: NREC guidance on use of biological samples and associated data - https://www.nrecoffice.ie/guidance-on-use-of-biological-samples-and-associated-data/
- The NREC-CT noted that pg. 30 of the Main ICF states that participants may undergo whole genome / whole exome sequencing and requested the following:
    - Genomic sequencing is confined to genes involved in the disease being treated or related diseases and /or genes involved in the metabolism of the medicines being used in the trial and this elucidated in the ICF
    - Explicit consent, including outlining the risks entailed in such analysis being performed, is added to the ICF (no risks are listed on pg 41- has this been given due consideration?)
    - The possible ownership of such data by private or commercial interests and that this elucidated in the ICF.
    - The right to withdraw genetic data, and clear information on how to do so, must also be provided in the ICF.
    - Clarification is provided in the ICF on the storage location of genetic material and its associated data.
    - For guidance, please see HSE National Policy for Consent in Health and Social Care Research (V2.0, 2024). Dublin: Health Service Executive https://www2.healthservice.hse.ie/organisation/national-pppgs/hse-national-policy-for-consent-in-health-and-social-care-research

2025-522216-17-00

Institutions: St James's Hospital

Study title: A multi-part, adaptive, Phase 1, first time in human study in healthy participants and participants with atopic dermatitis (AD) to assess the safety, tolerability, pharmacokinetics (PK) of single ascending (SAD), multiple ascending doses (MAD) and selected dose of SYX-5219 (AD Participants)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations

1. **Financial arrangements**

- The NREC-CT noted that compensation for participants loss of income as well as travel related reimbursement for one caregiver may be considered (pg17 Main PISCF) but that these are not included in the Compensation for Trial Participants Form. In addition, monetary payments for study visits, biopsies, and diary completion are outlined in the Compensation for Trial Participants Form but omitted from the Main PISCF. The Committee requested that both documents are aligned.

2. Subject information and informed consent form

- If applicable, the Sponsor is requested to submit any Part 2 documentation that require updates as a result of the Part 1 Assessment. Please include detail of the Part 1 consideration that triggered the update to the Part 2 documentation.
- The National Office requests that all documentation provided in response to RFI is presented in an accessible and searchable format (Word or original PDF). We are unable to accept scanned documents (including documents modified using Optical Character Recognition) as these documents cannot be optimised for use with assistive software.
- The NREC-CT noted a reference to the potential use of a patient concierge service e.g., Greenphire (Main ICF, pg17). The Committee request the submission of applicable consenting documentation for the use of this third-party vendor in the event that use of this service is confirmed.

2025-521697-34-00

Institutions: Cork University Hospital, Children's Health Ireland

Study title: A Phase 3, Double-Blind, Placebo-Controlled, Randomized Study to Assess the Safety of Epicutaneous Immunotherapy with DBV712 250 µg in 1-through 3-year-old Children with Peanut Allergy

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations

1. Financial arrangements

- The NREC- CT noted that participants/carers will not be reimbursed for accommodation in the Compensation Form (p1). The Committee requested that reimbursement of overnight accommodation expenses is considered for participants/carers if required and if included, that it is elucidated in the Compensation Form and PISCF's.

2. Subject information and informed consent form

- If applicable, the Sponsor is requested to submit any Part 2 documentation that require updates as a result of the Part 1 Assessment. Please include detail of the Part 1 consideration that triggered the update to the Part 2 documentation.

- The National Office requests that all documentation provided in response to RFI is presented in an accessible and searchable format (Word or original PDF). We are unable to accept scanned documents (including documents modified using Optical Character Recognition) as these documents cannot be optimised for use with assistive software.
- The NREC-CT noted that throughout the PISCF's the term "you" may refer to the legal guardian or to the study participant (pg 1 Parent DBPC PISCF and pg 1 Parent OLE PISCF). The Committee request that a grammatical distinction is made between the legal guardian and the study participant in all relevant PISCF's to ensure readability and facilitate informed consent.
- The NREC-CT considered the PISCF to be comprehensive but long. The Committee requested that a brief plain English executive summary of the salient points of the study be included at the beginning of the PISCF. Additionally, please clarify the rationale for submitting the document entitled 'L2_IE_Other Subject Material_Plain Language Summary - EPITOPE study'
- The NREC-CT noted that the future use of data / samples (including genetic research) is not described in line with regulations / best practice in the Main PISCF. The NREC-CT requested that future use of samples / personal data is sufficiently explained to participants in the PISCF documents 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 made optional
    - it should be confined to a specified disease, related diseases or drug under study in this trial (pg 8 "Look at the effect of the study medication and/or other medications on the body")
    - optional future research is made into a separate and explicit consent item in the Informed Consent section of the Main PISCF, with separate participant information section and signatures section, so it is distinct from the main consent to participate in the research.
    - The PISCF should also make it clear to participants that subsequent research ethics review will be sought for specific research once clearly defined. For further guidance, please see: NREC guidance on use of biological samples and associated data - https://www.nrecoffice.ie/guidance-on-use-of-biological-samples-and-associated-data/

2024-516030-35-00 SM-3

Institutions: University Hospital Galway, University Hospital Waterford, Beaumont Hospital

Study title: A Phase 3, randomized, open-label study of belantamab mafodotin administered in combination with lenalidomide and dexamethasone versus daratumumab, lenalidomide, and dexamethasone in participants with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplantation (TI-NDMM)-DREAMM-10

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

2024-514173-22-00 SM-6

Institutions: Children's Health Ireland Crumlin, University Hospital Limerick, Cork University Hospital, St Vincent's University Hospital, Children's Health Ireland Temple Street

Study title: A Phase 3, Open-label Study Evaluating the Long-term Safety and Efficacy of VX-121/TEZ/D-IVA Combination Therapy in Subjects With Cystic Fibrosis

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

2023-504807-94-00 SM-10

Institutions: Mater Misericordiae University Hospital

Study title: First-in-Human Study of STX-478, a Mutant-Selective PI3Kα Inhibitor as Monotherapy and in Combination With Other Antineoplastic Agents in Participants With Advanced Solid Tumors

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations raised
1. Subject information and informed consent form

- If applicable, the Sponsor is requested to submit any Part 2 documentation that require updates as a result of the Part 1 Assessment. Please include detail of the Part 1 consideration that triggered the update to the Part 2 documentation
- The National Office requests that all documentation provided in response to RFI is presented in an accessible and searchable format (Word or original PDF). We are unable to accept scanned documents (including documents modified using Optical Character Recognition) as these documents cannot be optimised for use with assistive software.
- The NREC-CT noted that page 45 of the Main Monotherapy PIS-ICF includes a witness signature line. The Committee requests information be added to all

relevant PISCF's explaining the context where a witness signature would be needed (as per CTR: Annex I,L 62(b)).

- The NREC-CT noted that an optional biopsy may be performed at the end of treatment (Main Monotherapy PIS-ICF pg 52) but that additional explanatory information was lacking in the PISCF. The Committee requested that further information be provided on the biopsy procedure, in all relevant PISCFs, with regard to the type of analysis to be performed, in order to facilitate informed consent.

2024-511754-41-00 SM-4

Institutions: St Vincent's University Hospital, Beaumont Hospital, Cork University Hospital, Mater Misericordiae University Hospital

Study title: A Phase 2, Multi-Center, Randomized, Double-Blind, Controlled Trial Evaluating the Safety and Efficacy of ENV-101 in Patients with Lung Fibrosis (WHISTLE-PF Trial)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations raised

1. **Subject information and informed consent form**

- If applicable, the Sponsor is requested to submit any Part 2 documentation that require updates as a result of the Part 1 Assessment. Please include detail of the Part 1 consideration that triggered the update to the Part 2 documentation
- The National Office requests that all documentation provided in response to RFI is presented in an accessible and searchable format (Word or original PDF). We are unable to accept scanned documents (including documents modified using Optical Character Recognition) as these documents cannot be optimised for use with assistive software.
- The NREC-CT noted that the future use of data / samples is not described in line with regulations / best practice on pg. 13/22 of the Main PISCF and pg. 4 of the Biological Samples Form. The NREC-CT requested that future use of samples / personal data is sufficiently explained to participants in the PISCF documents 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 PISCF should also make it clear to participants that subsequent research ethics review will be sought for specific research once clearly defined. For further guidance, please see: NREC guidance on use of biological samples and associated data - https://www.nrecoffice.ie/guidance-on-use-of-biological-samples-and-associated-data/

- The NREC-CT noted that the participant may not have access to the study drug after completion of the trial (Main ICF, pg 15). The Committee request that this is reconsidered, so that all participants benefiting from the study drug continue to have access.

- AOB:
  - None