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| **Committee:** | Southern Health and Disability Ethics Committee |
| **Meeting date:** | 8th November 2022 |
| **Zoom details:** | 96507589841 |

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| **Time** | **Review Reference** | **Project Title** | **Coordinating Investigator** | **Lead Reviewers** |
| 10.30-11.00am | 2022 FULL 13542 | A Study Evaluating the Long-term Safety and Efficacy of VX-121 Combination Therapy (VX20-121-104) | Dr Mark O'Carroll | Mr Dominic Fitchett and Associate Professor Mira Harrison-Woolrych |
| 11.00-11.30am | 2022 FULL 12932 | ABTECT - Maintenance | Dr Vivek Tharayil | Mr Dominic Fitchett and Dr Devonie Waaka |
| 11.30am-12.00pm | 2022 FULL 13686 | A Phase 3 Study Comparing Epcoritamab plus R-CHOP v R-CHOP in Newly diagnosed DLBCL | Dr Peter Ganly | Ms Dianne Glenn and Associate Professor Nicola Swain |
| 12.00-12.30pm | 2022 FULL 13712 | NEOLEV3 High dose levetiracetam for the treatment of neonatal seizures | Doctor Cynthia Sharpe | Mr Dominic Fitchett and Associate Professor Mira Harrison-Woolrych |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Devonie Waaka | Non-lay (Intervention studies) | 18/07/2016 | 18/07/2019 | Present |
| Assc Prof Mira Harrison-Woolrych | Non-lay Intervention/Observational studies) | 28/06/2019 | 28/06/2020 | Present |
| Mr Dominic Fitchett | Lay (the Law) | 05/07/2019 | 05/07/2022 | Present |
| Ms Amy Henry | Non-lay (Observational studies) | 13/08/2021 | 13/08/2024 | Present |
| Ascc. Prof Nicola Swain | Non-lay Intervention/Observational studies) | 22/12/2021 | 22/12/2024 | Present |
| Ms Dianne Glenn | Lay (Consumer/Community perspectives) | 08/07/2022 | 08/07/2025 | Present |
| Ms Neta Tomokino | Lay (Consumer/Community perspectives) | 08/07/2022 | 08/07/2025 | Present |

## Welcome

The Committee opened with a karakia at 10.00am. It was noted that there was no Chair presiding over Southern. The Committee nominated Mr Dominic Fitchett to be Acting Chair for Southern until a Chair is appointed, and this was approved by consensus.   
  
The Chair opened the meeting at 10:15am and welcomed Committee members, noting that apologies had been received from Ms Neta Tomokino and Ms Amy Henry.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

## Confirmation of previous minutes

The minutes of the meeting of 11 October 2022 were not confirmed, subject to further review by the Committee and approval of the Chair. These will be uploaded once confirmed by the Committee online.

## New applications

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| **1** | **Ethics ref:** | **2022 FULL 13542** |
|  | Title: | A Phase 3, Open-label Study Evaluating the Long-term Safety and Efficacy of VX-121 Combination Therapy in Subjects With Cystic Fibrosis (VX20-121-104) |
|  | Principal Investigator: | Dr Mark O’Carroll |
|  | Sponsor: | Vertex Pharmaceuticals Incorporated |
|  | Clock Start Date: | 27 October 2022 |

Dr Mark O’Carroll was present via videoconference for discussion of this application.

Potential conflicts of interest

The Chair asked members to declare any potential conflicts of interest related to this application.

No potential conflicts of interest related to this application were declared by any member.

Summary of resolved ethical issues

The main ethical issues considered by the Committee and addressed by the Researcher are as follows.

1. The Researcher explained that no participants will receive placebo, participants will receive 96 weeks of VX121 drug.
2. The Committee asked about the new medicine device and if the Researcher sees any possible risks with use of the device. The Researcher explained that studies have been done before with this device used at home visits and no risks have been shown for participants.
3. The Committee noted that ethnicity data collected should include data that reflects the New Zealand population. Should this differ from ethnicity groups required per protocol for the eCRF, please collect additional data at a site level for submission to HDEC with the final study report. The researcher confirmed that this was the site’s usual practice.
4. The Committee queried how the Participant Information Sheet and Consent Form Addendum was intended to be used. The researcher confirmed it was to be used in the event remote visits or home care were required.

Summary of outstanding ethical issues

The main ethical issues considered by the Committee, and which require addressing by the Researcher are as follows.

1. The Committee noted that the response to D8 states all individuals will provide informed consent, however those under 16 may lack the capacity to do so. The Committee asked for clarification around the processes for determining capacity to provide full informed consent for those aged under 16.
2. The Committee asked if participants will be able to use the trial drug after the study is completed. The Researcher explained participants will not have access to the trial drug. The Committee asked for an ethical justification for not providing ongoing access to participants experiencing therapeutic benefit from the study drug at study completion. The researcher confirmed they will raise the issue with the Sponsor to see if compassionate access can be arranged.
3. The Committee noted that the description of possible future use of tissue for genetic biomarker analysis is too broad to be mandatory and noted that for at least one of the parent studies pharmacogenomic analysis was optional. The Researcher explained that this is most probably an error as there is no need for the mandatory genetic analysis for this study. The Researcher confirmed they will provide an optional PISCF for this.
4. The Committee noted that B17 of the application form states that participants will not have access to individual study test and procedure results due to blinding. As this is an open label study, please confirm that participants will have access to individual results.
5. The Committee noted that the response to B17.3 in the application form addressed individual results, not the results of the study overall. Please confirm that all participants will be offered the option of receiving a lay summary of study results, once these are available.
6. The Committee noted that the response to E12 of the application form states that compensation would not be available for all entitlements available through ACC and reminded the researcher that HDEC approval is contingent on confirmation that ACC-equivalent compensation be provided. Please confirm that all entitlements listed in E12 will potentially be available.
7. The Committee requested that the minor error in the contents section of the Data and Tissue Management Plan (‘bookmark not defined’) be corrected.
8. The Committee requested evidence of professional indemnity for the Coordinating Investigator (i.e. MPS Certificate of Membership or similar).
9. The Committee requested Sponsor authorisation be completed.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

Main PIS/CF:

1. Please review and simplify, using lay terms throughout (e.g., 'blood' rather than 'serum').
2. On page 5, there is no mention of genetic testing, and no mention that biomarker samples will be used for purposes outside of the current study. Please state clearly that biomarkers will be used for other research related to the study drug and/or disease.
3. Please state whether participants will be informed of the results of the exploratory biomarker research.
4. On page 8, please make it clear that karakia will not be available at time of tissue destruction.
5. On page 11, please amend the typo in the following sentence: “You should not donate sperm from the first dose of the VX-121/TEZ/D-IVA in the until at least 90 days after the last dose of study medication.”
6. On page 12, please delete references to co-payments and deductibles, IBAN, SWIFT BIC, etc as they are not applicable to New Zealand participants.
7. On page 12, please delete references to Greenphire at a site level if there is no plan to use this service.
8. On page 14, please amend the information regarding access to medical records as it is currently better described on page 15. Please ensure information is presented once only.
9. On page 19, please insert ‘type of tissue’ where bracketed.
10. Please amend the information regarding ongoing use of data and tissue; it is repeated several times during the document and is not consistent. This information only needs to be presented once.

Optional Genetic PISCF:

1. Please provide an optional PISCF for the exploratory genetic analysis noted in the application form and protocol.
2. Please state in lay language what genes and DNA are, and that genetic information is shared by blood relatives.
3. Please state the breadth of genetic analysis, including whether the participant's entire genetic code will be sequenced / analysed.
4. Please state whether the genetic research undertaken could have implications for the participant or his/her blood relatives.
5. Please state whether there is any risk of full or familial matches across different genetic databases.
6. Please state whether participants will be informed of the results of the optional research.

Adolescent PIS/CF:

1. The form currently requires a significant overhaul using shorter sentences, simpler lay language, and more targeted information.
2. Please remove the statement that treatment may make them feel "afraid, uncomfortable and hurt".
3. Please add an assurance of privacy when discussing reproductive risks. Please include a statement that parents do not need to be informed.

**Decision**

This application was *provisionally approved* by consensus, subject to the following information being received:

1. Please address all outstanding ethical issues, providing the information requested by the Committee.
2. Please update the data management plan *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15a).*
3. Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Dominic Fitchett and Associate Professor Mira Harrison-Woolrych.

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| **2** | **Ethics ref:** | **2022 FULL 12932** |
|  | Title: | A randomized, double-blind, multicenter phase III study to evaluate the long-term efficacy and safety of ABX464 25 mg or 50 mg once daily as a maintenance therapy in subjects with moderately to severely active ulcerative colitis |
|  | Principal Investigator: | Dr Vivek Tharayil |
|  | Sponsor: | Abivax |
|  | Clock Start Date: | 27 October 2022 |

Katherine Denton was present via video conference for discussion of this application.

**Potential conflicts of interest**

The Chair asked members to declare any potential conflicts of interest related to this application.

No potential conflicts of interest related to this application were declared by any member.

**Summary of resolved ethical issues**

The main ethical issues considered by the Committee and addressed by the Researcher are as follows:

1. The Committee asked the researcher to outline processes in place to ensure adequate mental health follow-up of participants whose responses indicate significant mental health issues, as the response to E3.2 of the application form states only that the participant will be withdrawn from the study. The Researcher explained that participants would be referred to the mental health team at each locality on site.
2. The Committee asked about the risk of ‘worsening of UC’ in the participation information sheet and asked whether participants’ disease had worsened after dosing. The Committee noted that this risk would appear to be a key concern to those considering whether to participate in this study, and that there is little about it in the participant-facing information. The Researcher explained that some participants’ UC had worsened in previous studies, but it is unclear whether this may have been participants allocated to placebo. The Researcher confirmed that the study team would look at the data from previous studies and will amend PISCF wording to better reflect the risk.
3. The Committee noted that a pregnant participant/partner participant information sheet/consent form should only be submitted as an amendment in the event that a pregnancy occurs so it can be fit-for-purpose. As such, these have not been approved for use with the current submission.

**Summary of outstanding ethical issues**

The main ethical issues considered by the Committee, and which require addressing by the Researcher are as follows:

1. The Committee noted that ethnicity data collected should include data that reflects the New Zealand population. Should this differ from ethnicity groups required per protocol for the eCRF, please collect additional data at a site level for submission to HDEC with the final study report.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

1. Please review for formatting errors such as page numbering.
2. On pages 2/3, please fill in length of visits (‘XX’ in several places).
3. On page 2/3, please insert a lay version of the protocol study design diagram (page 32 of the protocol) to illustrate treatment arms more clearly.
4. On page 3, please clearly explain the difference between 'relapse' and 'worsening of disease'.
5. On page 7, please remove echo information as it is not applicable to the main study.
6. On page 9, please check table footnotes (‘e’ should be ‘f’ re echocardiogram at bottom of page).
7. On page 11, please advise that a karakia won’t be available at time of tissue destruction.
8. On page 14, please remove repeated paragraph (end of page).
9. On page 23, please remove yes/no tick boxes for the statements about withdrawal of information and informing GP.
10. Please state approximately how long it will take to complete each set of questionnaires and diary entries.
11. Please state whether the colonoscopy requires a separate clinic visit, where the procedure will be performed, and the visit duration, etc.
12. Please delete repeated information regarding pregnancy testing.
13. Please delete references to notifiable diseases (use of data section); none are tested for in this study (as per protocol).
14. If it is not optional for participant's data to be used for future related and/or unrelated research, please delete 'if you agree' on p17. If it is optional, please add an optional tick box to the applicable clause on the consent page.
15. Please simplify reasons for withdrawal from study.
16. Please replace 'pseudonymised' with 'coded' or explain the term in lay language.
17. Please remove PIS/CF template instructional statement from consent page.

**Decision**

This application was *provisionally approved* by consensus, subject to the following information being received:

1. Please address all outstanding ethical issues, providing the information requested by the Committee.
2. Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Neta Tomokino and Dr Devonie Waaka.

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| **3** | **Ethics ref:** | **2022 FULL 13686** |
|  | Title: | A Phase 3, Randomized, Open-Label Study to Evaluate Safety and Efficacy of Epcoritamab in Combination with R-CHOP Compared to R-CHOP in Subjects with Newly Diagnosed Diffuse Large B-Cell Lymphoma (DLBCL) |
|  | Principal Investigator: | Dr Peter Ganly |
|  | Sponsor: | AbbVie |
|  | Clock Start Date: | 27 October 2022 |

Helen McDermott was present via videoconference for discussion of this application.

**Potential conflicts of interest**

The Chair asked members to declare any potential conflicts of interest related to this application.

No potential conflicts of interest related to this application were declared by any member.

**Summary of resolved ethical issues**

The main ethical issues considered by the Committee and addressed by the Researcher are as follows:

1. The Committee noted that a pregnant participant/partner participant information sheet/consent form should only be submitted as an amendment in the event that a pregnancy occurs so it can be fit-for-purpose. As such, these have not been approved for use with the current submission.

**Summary of outstanding ethical issues**

The main ethical issues considered by the Committee, and which require addressing by the Researcher are as follows.

1. The Committee requested that processes are in place to mitigate the risk of patients feeling undue pressure to participate as a result of an existing doctor-patient relationship. While it is appropriate for the Investigator / clinician to initially approach the patient about the study, please ensure another member of the research team conducts the remainder of the recruitment process.
2. Biomarker analysis is described in the application form as both mandatory (F4.1) and optional (F9) and includes genetic analysis. The described breadth of research is very similar for both. The protocol states samples will be used 'to evaluate known and/or novel disease-related or drug-related biomarkers. Some of these samples may be optional'. No guidance is provided regarding which samples are mandatory. Please clarify which samples are mandatory, whether 'disease-related' is restricted to DLBCL or encompasses any disease, and whether 'drug-related' is restricted to the study drugs or to any drug.
3. EuDRACT is not in itself a WHO-approved clinical trials registry (CTR). Please confirm whether the study is also registered with the EU CTR or another WHO-approved CTR.
4. Section 6.1 of the Data and Tissue Management Plan (DTMP) states that participants will be notified of privacy breaches only 'if the Privacy Breach is a Notifiable Privacy Breach'. Please ensure participants are informed of any privacy breach, unless a justification is accepted by HDEC for not doing so.
5. Both participant information sheets state that tissue is only going to Labcorp in Singapore, however seven overseas laboratories are listed as being used for the study on pages 9 and 10 of the DTMP. Please clarify what is intended and amend the documentation accordingly.
6. The Committee noted that ethnicity data collected should include data that reflects the New Zealand population. Should this differ from ethnicity groups required per protocol for the eCRF, please collect additional data at a site level for submission to HDEC with the final study report.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

Main PIS/CF:

1. Please correct page numbering; numbering reverts to ‘1’ following the study assessment table.
2. The PIS/CF states participants in the investigational arm will be hospitalised OR required to stay within a 30-minute commute of the hospital. Clarify whether New Zealand participants will be provided with the option to commute; and if applicable, whether accommodation costs will be reimbursed.
3. Please review for lay language, i.e., define a molecule.
4. Page 3 states there are 315 research centres worldwide. Please include where the two study sites are in New Zealand.
5. On page 2, most of the information under Voluntary Participation is a repeat of information on page 1. Please delete all repeated information.
6. On page 3, please replace 'monotherapy' with lay term (i.e. 'alone').
7. Please review information about required testing for infection on page 5. If not required in New Zealand, delete. If required, delete 'if required per local regulations' and correct reference to 'state law' to be specific to New Zealand. See also information provided on page ‘1’ and amend as required, ensuring 'also known as the AIDS virus' is deleted from the description of HIV.
8. On pages 5 and 6, neurologic assessment is described twice. Please delete redundant text.
9. On page 7, please delete teaspoon blood references and use millilitres.
10. On page 7, please explain what 'biomarker research' is in lay terms the first time this is mentioned.
11. Please state that genes are shared with blood relatives. State whether genetic research may include analysis of the entire genetic code. State whether there are any risks of matching genetic data across databases (e.g., law enforcement or commercial databases).
12. Please clearly explain the circumstances under which 'The study doctor and research team may share your Personal Data .... with regulatory authorities in countries around the world and with the ethics committees responsible for oversight of this research study'. If this is limited to review on site for audit purposes, this should be stated.
13. Justify to the committee the statement "Please note that your access to your research records may be suspended during your participation in the research study...”; it is unclear how access could negatively impact scientific validity in an open label study. If not applicable, please delete.
14. In the data section, please address risk of privacy breach.
15. On page 17, please delete the statement “Decisions made in the commercial interests of the sponsor or by local regulatory/health authorities" as this is not a valid reason for study termination in New Zealand.
16. On page 17, the following “The drug/treatment/device being shown to work and not need further testing" is stated as a reason for study termination. Please clarify to the committee whether participants receiving therapeutic benefit at the time of study termination would have ongoing access to IMP.
17. Please delete optional tick boxes for GP notification of study enrolment and abnormal results; this is a mandatory component of study participation (consent form).
18. Please insert an optional clause for receipt of lay summary of study results (consent form).
19. Please delete signature space for legally authorised representative; proxy consent is not approved for this study (consent form).
20. Under MRI scans, to objects and devices, please add "brassieres with under breast metal inserts/wires".
21. Under CRS, "steroids" is used again - if not clarified earlier do so here, in lay terms and/or examples.
22. Under ICANS, 6th line - after "fatal" please put a full stop and start next sentence with "A patient who had......"
23. Under risks from other study medicines / side effects seen, 4th line: please remove brackets around (country) and insert "New Zealand".
24. In the box under Serious side effects second bullet point, please provide a common name in brackets for "Cytomegalovirus" as you have for others.
25. In both places where hair loss is mentioned, please insert in brackets (alopecia).
26. Under Prednisone, please remove the last bullet point as that is also the fourth bullet point.
27. Under "Who will receive my Personal Data" third paragraph: please remove "and/or device".
28. Where "your country" is stated, please replace with "New Zealand".
29. Please note that 56% of those receiving Epcoritamab experience Cytokine Release Syndrome (CRS). Please provide more information about the context and risk for participants, including how this side effect might be managed.
30. Please use the [HDEC template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-reproductive-risks-v.3.0-july2022.docx) for reproductive risks in the PIS.

Optional PIS/CF:

1. The aims of the study are repeated (on pages 2 and 3). Please include one explanation only.
2. On page 2, the text states optional research is for tumour tissue samples only; please confirm whether this is correct.
3. State that genes are shared with blood relatives. State whether genetic research may include analysis of the entire genetic code. State whether there are any risks of matching genetic data across databases (e.g. law enforcement or commercial databases).
4. On page 4, please delete repeated information under 'Do I have to take part in this research study'.
5. On page 5, please explain what new 'safety information that may be related to your participation in the research' would continue to be collected should a participant withdraw from optional biomarker analysis. Delete if not applicable to the optional PIS/CF.
6. In the consent form, please delete signature space for legally authorised representative; proxy consent is not approved for this study.
7. At the bottom of page 1 please remove the 2nd "are".
8. Please clarify the possibility of karakia when samples are sent overseas.

**Decision**

This application was *provisionally approved* by consensus, subject to the following information being received:

1. Please address all outstanding ethical issues, providing the information requested by the Committee.
2. Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
3. Please update the study protocol, taking into account the feedback provided by the Committee. (National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).

After receipt of the information requested by the Committee, a final decision on the application will be made by Associate Professor Nicola Swain and Dianne Glenn.

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| **4** | **Ethics ref:** | **2022 FULL 13712** |
|  | Title: | NEOLEV3: A Phase IIb Dose Escalation Study of Levetiracetam in the Treatment of Neonatal Seizures |
|  | Principal Investigator: | Dr Cynthia Sharpe |
|  | Sponsor: | University of Minnesota School of Medicine |
|  | Clock Start Date: | 27 October 2022 |

Dr Cynthia Sharpe was present via videoconference for discussion of this application.

**Potential conflicts of interest**

The Chair asked members to declare any potential conflicts of interest related to this application.

No potential conflicts of interest related to this application were declared by any member.

**Summary of resolved ethical issues**

The main ethical issues considered by the Committee and addressed by the Researcher are as follows.

1. The Committee noted that this is a resubmission of a previously Provisionally Approved study and commended the work put in by the Researchers to address the changes requested in the original review.
2. The Researchers confirmed that the study is undergoing clinical trial registry registration.
3. The Committee noted that D.14 of the application form states that parents are enrolling their child under the best interest test. The Committee clarified with the Researcher that this is not the case; parents are instead providing consent on behalf of their child.

**Summary of outstanding ethical issues**

The main ethical issues considered by the Committee, and which require addressing by the Researcher are as follows.

1. The Committee requested the following changes to the Data Management Plan (DMP) *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15a)*:
   1. Please remove the note to researchers on page 3 as this is part of the template.
   2. The Committee noted Section 4 states that de-identified health data is being collected and used for the study even if consent is not obtained. After discussion, this was clarified that this is anonymised information to keep a record of those who screen-fail, and only date of referral and reason for not participating (not consenting or not eligible) is recorded and kept. The Committee requested this is updated in the DMP and protocol to reflect that the data collected is anonymous.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

1. Please review for technical terms and make them more lay-friendly (i.e. use the drug name as opposed to the abbreviation letters).
2. On page 2, with respect to the optional part of the study, please clarify whether the information provided to external researchers/companies would be identifiable.
3. On page 4, please report on Levetiracetam potential side effects and frequencies observed from previous study data.
4. On page 7, please replace New Zealand Health and Disability Ethics Committee with Southern Health and Disability Ethics Committee.

**Decision**

This application was *approved* by consensus, subject to the following non-standard conditions:

* please address all outstanding ethical issues raised by the Committee
* please update the Participant Information Sheet and Consent Form, taking into account the feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17)*
* please update the study protocol, taking into account the feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7)*
* please update the data management plan, taking into account the feedback provided by the Committee. (National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15a).

## General business

1. The Chair reminded the Committee of the date and time of its next scheduled meeting:

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| **Meeting date:** | 13 December 2022 |
| **Zoom details:** | To be determined |

The following members tendered apologies for this meeting.

* Associate Professor Mira Harrison-Woolrych
* Associate Professor Nicola Swain

1. **Review of Last Minutes**

The minutes of the meeting of 27th September 2022 were not confirmed, subject to further review by the Committee and approval of the Chair after some issues were identified. These will be uploaded once confirmed by the Committee.

1. **Matters Arising**
2. **Other business**
3. **Other business for information**
4. **Any other business**

The meeting closed at 12.30pm