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| **Committee:** | Southern Health and Disability Ethics Committee |
| **Meeting date:** | 14 March 2023 |
| **Zoom details:** | 965 0758 9841 |

| **Time** | **Review Reference** | **Project Title** | **Coordinating Investigator** | **Lead Reviewers** |
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| 10.30-11.00am | 2023 FULL 15177 | DEPOSITION | Dr Shay McGuinness | Ms Catherine Garvey and Associate Professor Mira Harrison-Woolrych |
| 11.00-11.30am | 2023 FULL 15361 | H. pylori in Aotearoa New Zealand | Associate Professor James Stanley | Ms Dianne Glenn and Dr Devonie Waaka |
| 11.30am-12.00pm | 2023 FULL 15109 | A randomised trial comparing endoscopic versus surgical treatment for reflux | Doctor Cameron Schauer | Mr Dominic Fitchett and Ms Amy Henry |
| 12.00-12.30pm | 2023 FULL 12278 | Cervical spine antibiotic concentration | A/Professor Joe Baker | Ms Dianne Glenn and Associate Professor Mira Harrison-Woolrych |
|  | *Break* |  |  |  |
| 1.00-1.30pm | 2023 FULL 15150 | Study to Evaluate the Safety, Efficacy, Pharmacokinetics, and Pharmacodynamics of ABBV-552 in Participants with Mild Alzheimer's Disease | Dr Nigel Gilchrist | Ms Catherine Garvey and Dr Devonie Waaka |
| 1.30-2.00pm | 2023 FULL 15247 | INSMED 211 | Dr Lutz Beckert | Mr Dominic Fitchett and Associate Professor Nicola Swain |
| 2.00-2.30pm | 2023 FULL 15441 | INSMED 212 | Dr. Lutz Beckert | Mr Dominic Fitchett and Associate Professor Nicola Swain |

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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 | Apology |
| Ms Catherine Garvey  | Lay (the Law)  | 19/03/2019  | 19/03/2022  | Present  |

## Welcome

The Chair opened the meeting at 10.00am and welcomed Committee members, noting that apologies had been received from Ms Neta Tomokino.

The Chair noted that it would be necessary to co-opt members of other HDECs in accordance with the Standard Operating Procedures. Ms Catherine Garvey confirmed their eligibility and were co-opted by the Chair as a member of the Committee for the duration of the meeting.

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 14 February 2023 were confirmed.

## New applications

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| **1**   | **Ethics ref:**   | 2023 FULL 15177 |
|   | Title:  | Decreasing Postoperative Blood Loss by Topical vs. Intravenous Tranexamic Acid in Open Cardiac Surgery (DEPOSITION) Trial |
|   | Principal Investigator:  | Dr Shay McGuinness |
|   | Sponsor:  | Population Health Research Institution of Canada |
|   | Clock Start Date:  | 14 March 2023 |

Dr Shay McGuinness and Dr Rachael Parke were 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 asked about the recruitment process and how potential participants will be approached. The Researcher explained that potential participants will be seen at their usual pre-op meeting on Wednesday mornings with the rest of potential participants being hospital cases that will be approached the day before surgery. The Committee was assured that every potential participant will have 24 hours’ notice to decide to be a part of the study.
2. The Committee asked if there is someone from the research team who is not involved in the participants clinical care who would be consenting the potential participant. The Researcher explained that most of the consent process is done by the research team of which are 7 research coordinators not involved in their direct care.
3. The Committee asked about future unspecified research and how study data may be used in the future. The Researcher explained that beyond secondary analysis by the trial investigators it will not be used by anybody else.
4. The Committee asked about the study sponsor. The Researcher clarified that Population Health Research Institution of Canada is the global sponsor for this trial

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 the following about the Data Management Plan (DMP):
	1. The DMP and participant information sheet/consent form refer to the Study Sponsor as Population Health Research Institute, Canada, however the application form states the study has no local or global sponsor and Sponsor authorisation has not been provided. Please amend incorrect documentation accordingly.
	2. Section 8.5 states data may be used for future unspecified research; Section 11.2.1 states no future unspecified research is planned. Please clarify what is intended and amend the incorrect statement.
2. The Committee noted that the peer review document submitted was a funding letter instead. Please provide a full independent peer review.

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

1. Please amend the lay study title to describe the study aims in simple terms.
2. Please proofread for typos and formatting errors and use lay friendly terms when possible.
3. Please be consistent with use of “tranexamic acid” and “TxA”, it is defined as TxA on page 1, use TxA after that or remove the definition and just use tranexamic acid.
4. On page 2, please state the number of New Zealand participants.
5. On pages 1 and 2, please amend the section on the purpose of the study to be more lay friendly and clarify that the study is directly comparing topical vs IV tranexamic acid during cardiac surgery.
6. On page 2, please delete the following sentence: "All patients routinely receive IV tranexamic acid..." from the ‘What is the Study Intervention’ section.
7. On page 2, please state that regardless of which group the participant is randomised to, they will receive an IV injection, and clarify that a placebo IV injection is administered to those who receive topical TxA.
8. On page 2, please delete the paragraph explaining randomisation
9. On page 2 please review and remove any duplication (i.e., “usual dose of 3 to 6 grams with a maximum of 10 grams”.
10. In the risks section, please include a statement that explains TxA is contraindicated for pregnancies, as it is important the participant is not pregnant before trial begins.
11. Please note that if there are any reproductive risks, or participants of reproductive age are excluded, this should be stated in the participant information sheet.
12. On page 5, please include a sentence that states coded study data could be used for future research, including research that might not be directly related to this study.

**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, taking into account the feedback provided by the Committee. (*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 Ms Catherine Garvey and Associate Professor Mira Harrison-Woolrych.

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| **2**   | **Ethics ref:**   | **2023 FULL 15361** |
|   | Title:  | Casting a long shadow: H. pylori prevalence in Aotearoa New Zealand |
|   | Principal Investigator:  | Associate Professor James Stanley |
|   | Sponsor:  | University of Otago |
|   | Clock Start Date:  | 02 March 2023 |

Dr Virginia Signal, Cheryl Davies, and Associate Professor James Stanley were 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 clarified that the approach of young participants would not purely be through their parents, the recruitment may be direct to the child or through their primary caregiver.
2. The Researcher noted that there would be interpreters available as necessary.
3. The Committee clarified the response rates of the study specifically in young people as was raised in the peer review. The Researchers replied that there was a lot of outreach undertaken in prior H. pylori studies that they would mirror in this study.

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 there was currently no possibility for younger participants to give independent informed consent. Please amend study documentation to ensure that younger participants with capacity to provide informed consent do so, rather than their parent / guardian consenting.
2. The Committee noted that for younger participants unable to provide independent informed consent, no assent form has been provided. This should be provided for review. Please ensure the assent form is appropriately worded and pitched for this younger audience.
3. The Committee requested inclusion of a statement in the study documentation that young people may be recruited independently from their parents.
4. The Committee noted that there is information in section 8.4 and 8.5 in the Data and Tissue Management Plan (DTMP) contradicting statements in the application form. Please amend these to be consistent, ensuring correct information is provided in both.
5. The Committee queried how verbal consent will be recorded. The Researcher noted that there would be audio recording, and the researcher would also document in writing that verbal consent had been obtained. The script provided for this consent process should be provided for review. Please also ensure the process for obtaining verbal consent is clearly described in the protocol.
6. The Committee requested provision of the researcher safety plan for home visits.

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

1. Please delete the statement in bold font at the beginning of the form.
2. Please clarify, for younger participants, who will be asked to complete the questionnaire – the participant or parent / caregiver.
3. Please clarify if younger participants will need to be present at interviews and conversations where the answers were being given primarily by the guardians/parents.
4. Please review the statements about future use of data and storage of data outside of New Zealand, as there are inconsistencies between the application and the DTMP.
5. Please remove the reference to “poo” on page 3 as the term “stool” has already been explained earlier in the form.
6. Please review the reimbursement to clarify if participants would be individually reimbursed.

**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 data and tissue 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, 14.16&14.17*).
4. Please provide a researcher safety plan (*National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.62*).

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

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| **3**   | **Ethics ref:**   | **2023 FULL 15109** |
|   | Title:  | Endoscopic Anti-Reflux Mucosal Ablation versus Nissen Fundoplication for Refractory Reflux: a blinded randomised control trial |
|   | Principal Investigator:  | Dr Cameron Schauer |
|   | Sponsor:  | Te Whatu Ora - Waitemata |
|   | Clock Start Date:  | 02 March 2023 |

Dr Cameron Schauer 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 clarified with the Researcher that the study is investigator initiated.
2. The Committee had the recruitment process clarified by the Researcher.
3. The Committee noted that there was no termination statement in any of the study documentation. The Researcher noted that there were very few cases in which this study would be terminated as there is no real risk as has been shown from use of this method in practice.
4. The Committee queried how the participants could consent if they were not provided the risks and therefore fully informed consent. The Researcher clarified that the participants would be consented for both procedures. The Committee suggested appending the standard patient information sheets of each treatment to the study participant information sheet.
5. The Committee clarified that there was no tissue to be collected for the study, any collected tissue would be standard of care.
6. The Committee noted that there would be no difference in the wait times between receiving treatment in the study or in the public system. The Researcher also noted that withdrawing from the study would not impact the timeline to treatment and the withdrawing participant would not be placed at the back of the queue for treatment.

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 queried who would be approaching potential participants. The Committee requested that someone not on the clinical team be provided to speak to potential participants during the recruitment process.
2. The Committee requested that the study be registered as a clinical trial with a WHO-approved Clinical Trial Registry.
3. The Committee noted that there was no consideration for Māori data sovereignty and other cultural considerations in the application. In future these should be considered.
4. The Committee requested that the researcher review the National Ethical Standards (para 9.7) for what is required of a protocol and amend the protocol accordingly
5. The Committee requested the following changes to the Data and Tissue Management Plan:
	1. The Committee requested a statement specifying where the data may be sent for analysis.
	2. Please remove reference to the colonoscopy.
	3. The Committee requested that de-identification of data should occur as the data is entered into the study spreadsheet. As NHI numbers and full date of birth are identifiable, they should be stripped from the study spreadsheet. The Researcher should keep a separate list linking personal identifiers to the participant’s assigned study number.
	4. Please remove any templated information in the Data Management Plan that is not relevant to the study.

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

1. Please include how many people will be in the study and what the chance is of receiving each procedure.
2. Please amend wording regarding “chosen” on page 2 to state “you have been invited”.
3. Please provide some justification of efficacy of each treatment. Stating the inability to compare the two presently is acceptable.
4. Please amend the wording of when participants will be notified as to which arm of the study they have been randomised into, as this will be prior to the study procedure.
5. Please include the risks of each treatment in the PIS/CFs. Please include some numerical data as to incidence of risk.
6. Please specify which follow up visits are study related and not standard of care.
7. Please specify how long visits will take and what will occur during these.
8. Please specify what will happen to data, who will have access, where it will be sent for analysis etc.
9. Please include a statement on reproduction as per the [HDEC reproductive risks template](https://ethics.health.govt.nz/guides-templates-and-forms/participant-information-sheet-templates/).
10. Please include an ACC statement. An example of one can be found in the HDEC Main PIS template.
11. Please include a statement that the participant’s General Practitioner will be informed of any incidental findings.
12. Please add the option for participants to receive a lay summary of the study results.
13. Please provide the PI contact details as the first point of call.
14. Please provide the site details.

**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*).
4. Please update the data and tissue 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, 14.16&14.17*).

After receipt of the information requested by the Committee, a final decision on the application will be made by Mr Dominic Fitchett and Ms Amy Henry.

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| **4**   | **Ethics ref:**   | **2023 FULL 12278** |
|   | Title:  | The effectiveness of bioimpedance analysis in determining appropriate surgical antibiotic prophylactic dosing in cervical spine surgery |
|   | Principal Investigator:  | Associate Professor Joseph Baker |
|   | Sponsor:  |  |
|   | Clock Start Date:  | 02 March 2023 |

No one from the research team 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 outstanding ethical issues

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

1. The Committee queried why karakia was not an option when this is standard now across most Te Whatu Ora localities. Please clarify.
2. The Committee queried if the samples would be identifiable and how the blood samples would be labelled. Please amend applicable study documentation as required.
3. The Committee queried how the consenting process will be performed. Please specify if the consent will be taken by those not involved in treatment to prevent undue influence.
4. The Committee noted that the study does not utilize Kaupapa Māori methodology.
5. The Committee requested the following changes to the Data and Tissue Management Plan (DTMP):
	1. Please remove all blue and red template text.
	2. Please delete section 7.3 and 8.3; no data or tissue will be collected anonymously.
	3. Please delete reference to GP, MOH and [laboratory manual] from section 8.1.
	4. Please delete final paragraph of Section 12 referencing anonymous data.
	5. Please amend section 12.1 as it is stated that no incidental findings are possible in the application form.

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

1. Please define technical terminology the first time it appears.
2. Please review the first sentence and consider using the study title to provide a lay explanation of the study.
3. Please review for typos and grammar (general) and delete repetition of information.
4. Please clarify what the GP may be contacted to provide; the application form states GPs will not be notified of study participation. If GP notification is possible, please make this clear in the body of the PIS.
5. Please consider inclusion of a photo or diagram of someone undergoing bio impedance analysis (page 2).
6. Please clarify what a 'small' piece of tissue is (page 2).
7. Please clarify whether tissue collection will lengthen surgery duration (page 2)
8. Please amend the section 'security and storage of your information' as it refers to coded data. This is being held locally and will not be sent to a sponsor (page 5)
9. Please describe bioimpedance analysis the first time it is mentioned. In the Purpose of the Study section, suggest explaining procedures in chronological order.
10. Please clarify how many muscle samples will be taken and at what time points as there is a discrepancy in this information between the PIS and protocol.
11. Please remove the following statement from the risks section: “There are no benefits to yourself from this study.”
12. Please consider underlining sub-headings.

**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*).
4. Please update the data and tissue 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, 14.16&14.17*).

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

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| **5**   | **Ethics ref:**   | **2023 FULL 15150** |
|   | Title:  | A Randomized, Double-blind, Placebo-controlled, Dose-finding Study to Evaluate the Safety, Efficacy, Pharmacokinetics, andPharmacodynamics of ABBV-552 in Participants with Mild Alzheimer's Disease |
|   | Principal Investigator:  | Dr Nigel Gilchrist |
|   | Sponsor:  | Abbvie Ltd |
|   | Clock Start Date:  | 02 March 2023 |

Dr Nigel Gilchrist and Deirdre Thompson were 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 confirmed that local sites will collect New Zealand-relevant ethnicity data.
2. The Application form states that participation will be reimbursed to an amount in New Zealand dollars as outlined in participant information sheet (PIS), but the PIS states there will be no reimbursement except for travel costs. The Researcher clarified that this is not a paid study, so only travel reimbursement will occur. The PIS contains the correct information.

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 based on the documentation provided, it is hard to tell the difference between breadth of analysis for mandatory genetic analysis and optional genetic analysis. The Committee’s position is that if a study includes mandatory genetic analysis, including genetic biomarker analysis, it must be directly related to the main study to fulfil study objectives. Where the breadth of potential analysis exceeds this, genetic analysis should be optional for New Zealand participants. The Committee requested the Sponsor provide further clarification on what is intended and amend study documentation for New Zealand participants accordingly.
2. The Committee noted that advertising materials to be used need to be submitted to HDEC prior to use as an amendment for review.
3. The Committee noted the following about the Data and Tissue Management Plan:
	1. Current wording states it is intended to inform participants only of notifiable privacy breaches. It would be expected that participants should be informed of any privacy breach involving their personal information. Please amend.
	2. Section 13 states that if a participant who has withdrawn from the study also 'withdraws permission for collection of Personal Information, a limited amount of new Personal Information may still be collected such as safety information that may be related to the participant’s participation in the study'. Please discuss the ethics of this approach, which is at odds with the response in G6 ('if withdrawn consent .... and the study team will stop collecting information').
4. EudraCT registration is not registration on a WHO-approved clinical trial registry. A search of sister site EU Clinical Trials Register failed to return any results. Please clarify which WHO-approved registry the study is registered with as this is a mandatory requirement.
5. The Committee requested the following further information regarding the Digital Neuro Signature testing:
	1. This seems quite onerous over time for something that is exploratory. Please state how realistic the 10-minute timeframe to complete is, especially without assistance.
	2. Please confirm as per the Digital Health Tool Qualification Form that the Sponsor will not have access to identifiable participant data. Clarify the position for Altoida who provides the device.

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

Main PIS/CF:

1. Review and simplify the lay title
2. Review use of lay language and simplify sentences where possible ('digital biomarker platform', 'cognitive', 'biomarker research', 'adverse events', 'concomitant therapy' 'WOCBP', efficacy, much of the contraception language, etc.) This is a PIS for those with mild cognitive impairment and this should be kept in mind.
3. Delete 'also known as the AIDS virus' and medical acronyms from the description of HIV and hepatitis (page 4).
4. Names of each questionnaire and clinical scale are not required - these add significant complexity (page 4).
5. Significantly simplify the schedule of activities, using lay terms (pages 6/7).
6. Provide the country location of each overseas laboratory (page 8).
7. Provide clearer information regarding mandatory genetic research (page 8), which should be limited to research directly related to the current study:
	1. What genes, DNA and RNA are.
	2. That a person's genetic code is unique to them, but closely shared with blood relatives.
	3. Whether the participant's entire genetic code will be recorded / analysed.
	4. Whether there is any risk of a participant being re-identified through their DNA sample (e.g., exact or familial matching across DNA databases).
	5. Whether genetic information may be shared or sold.
	6. Whether genetic data is shared with other researchers or used for any purposes outside of those required to fulfil the objectives of the main study.
8. Amend the cultural considerations section to specifically address issues regarding genetic research (page 9).
9. Rewrite the contraception section to make it relevant to a NZ lay population; sections of it appear to have been copied direct from the protocol. Given the age of the study population, this could all be significantly reduced to a statement that participants of reproductive potential should discuss required contraception options with the study doctor.
10. Address risk of privacy breach and risk of sending data overseas in privacy information section.
11. Include a consent statement agreeing to genetic research being undertaken on samples for purposes related to the current study only.

Partner PIS/CF

1. Amend lay title to reflect Main PIS/CF.
2. Review and simplify language used ('subject', 'adverse reactions', 'cognitive and functional').
3. Provide relevant information regarding number and length of clinic visits and telephone calls.
4. Amend text regarding lack of reimbursement should partner travel to clinic visits independently of participant to reflect that their travel expenses if they travel separately to the main participant is reimbursed.

**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 data and tissue 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, 14.16&14.17*).

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

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| **6**   | **Ethics ref:**   | **2023 FULL 15247** |
|   | Title:  | A Phase 2, Randomized, Double-Blind, Multicenter, Placebo-Controlled Study to Evaluate the Safety and Tolerability of Treprostinil Palmitil Inhalation Powder in Participants with Pulmonary Hypertension Associated with Interstitial Lung Disease (INSMED 211) |
|   | Principal Investigator:  | Dr Lutz Beckert |
|   | Sponsor:  | Insmed Incorporated |
|   | Clock Start Date:  | 02 March 2023 |

Olivia Brunel and Joanna Van Zyl were 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 both applications (2023 FULL 15247 (INSMED 211) and 2023 FULL 15441 (INSMED 212)) will be reviewed at the same time. Some comments may be applicable to both and this will be reflected in the minutes.

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 raised the following about the Application Form:
	1. The answer for this submission in D5 states that “the study will most likely be introduced to the potential participant by the investigator or sub investigator during a clinic visit”, which suggests that the investigator might “also provide non-research related clinical care or health/disability support for one or more participants in the study”, this is contrary to the answer given to question B21. Please explain answer, and recruitment process generally. The Researcher confirmed they could potentially be involved in the care of these potential participants and is the person undertaking the consent for all potential participants. The Committee noted that this could result in potential participants feeling undue pressure to participate. It is preferred that someone else in the study who was not their clinician obtain the informed consent.
	2. (E13) It appears the protocol numbers and study titles may have been mixed up on the insurance certificates provided for this study and the open label extension (2023 FULL 15441 - INSMED 212) – please check and correct if necessary.
	3. STUDY TERMINATION (E8). Note that therapeutic studies should not be terminated solely for commercial benefit. Amend study documentation to address this.
	4. ETHNICITY DATA COLLECTION (C16). Please ensure locally-relevant ethnicity data is collected in addition to that specified per protocol.
2. The Committee raised the following about the Data and Tissue Management Plan:
	1. Please address the 'Error? Reference source not found' messages throughout the data and tissue management plan.
	2. Please clarify what is meant by 'you will only be identified by your initials and your study number' in the participant information sheet/consent form (PIS/CF). The Committee queried if this refers to source data held at site, or de-identified data sent to the Sponsor. If the latter, initials should not be used; de-identified data should carry participant code only. Please also confirm that full date of birth will not be included in data sent to the Sponsor.
3. The Committee queried the intended study visit reimbursement amount as it currently states it will be different across sites with no justification provided. The Researcher clarified that the koha is $50 across all sites, and then the travel reimbursement will be different per site depending on travel needs and distance. The Committee requested this information is included in the PIS.
4. The Committee queried if participants will be informed of the open-label extension, and requested that it is mentioned in the PIS.

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

1. Please use a simple lay title as the main title (page 1)
2. Once a lay term has been used, bracketing with the technical term after each usage is not required.
3. Remove reference to federal law.
4. The Sponsor cannot stop the study solely for commercial benefit (page 2).
5. Give approximate number of NZ participants (page 3).
6. Listing components of the physical examination is not needed and can be removed (page 5).
7. The blood test information is incomplete and technical. Explain FSH and state what the blood tests are checking rather than using terms such as haematology, coagulation pro-BNP biomarker etc.
8. Replace 'hepatitis, HCV' with 'hepatitis B, hepatitis C' (page 5).
9. Simplify language used in table and remove lines that are not relevant to the participant.
10. On page 7, in relation to CT scanning process, the PIS refers to the radiographer and the technologist. If these are not different roles, please use the one title.
11. Bullet-point observed study drug AEs (pages 13/14). Note that these would usually precede procedural risks, which are all relatively minor. Please also move 'Notable Class Risks' to sit with risks of the study drug.
12. Explain what is meant by ‘of child-bearing potential' in lay terms (page 14).
13. The statement 'The Sponsor, and its representatives and companies acting on behalf of the Sponsor, HDEC and/or Medsafe might also review your records and information for other reasons' is too broad; use only the statement under 'Transferring your data to a third party' (page 17)
14. GP notification of study participation should be a mandatory component of study participation in a trial of this nature. Please delete 'With your permission...' (page 19)
15. Delete optional tick boxes for withdrawal of data and GP notification of study participation / abnormal results as these are mandatory for participation.

**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*).
4. Please update the data and tissue 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, 14.16&14.17*).

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

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| **7**   | **Ethics ref:**   | **2023 FULL 15441** |
|   | Title:  | An Open-Label Extension Study to Assess the Safety, Tolerability, and Effectiveness of the Long-Term use of Treprostinil PalmitilInhalation Powder in Participants with Pulmonary Hypertension Associated with Interstitial Lung Disease (INSMED 212) |
|   | Principal Investigator:  | Dr Lutz Beckert |
|   | Sponsor:  | Insmed Incorporated |
|   | Clock Start Date:  | 02 March 2023 |

Olivia Brunel and Joanna Van Zyl were 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 confirmed that everyone from this study is recruited from the Phase 2 participants.

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 raised the following about the Application Form:
	1. STUDY TERMINATION (E8). Note that therapeutic studies should not be terminated solely for commercial benefit. Amend study documentation to address this.
	2. ETHNICITY DATA COLLECTION (C16). Please ensure locally-relevant ethnicity data is collected in addition to that specified per protocol.
2. The Committee raised the following about the Data and Tissue Management Plan:
	1. Please address the 'Error? Reference source not found' messages throughout the data and tissue management plan.
	2. Please clarify what is meant by 'you will only be identified by your initials and your study number' in the participant information sheet/consent form (PIS/CF). The Committee queried if this refers to source data held at site, or de-identified data sent to the Sponsor. If the latter, initials should not be used; de-identified data should carry participant code only. Please also confirm that full date of birth will not be included in data sent to the Sponsor.
3. The Committee requested more information on the Sponsor’s plan for compassionate access beyond the open-label extension for those who have received therapeutic benefit.

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

1. The Committee noted that this PIS could be cut down a lot more as information can be referred to the main Phase 2 study and PIS. If not, any comments pertaining to INSMED 211 that pertain to this submission are applicable here as requests for changes which are outlined below.
2. Please use a simple lay title as the main title (page 1)
3. Once a lay term has been used, bracketing with the technical term after each usage is not required.
4. Remove reference to federal law.
5. The Sponsor cannot stop the study solely for commercial benefit (page 2).
6. Give approximate number of NZ participants (page 3).
7. Listing components of the physical examination is not needed and can be removed (page 5).
8. The blood test information is incomplete and technical. Explain FSH and state what the blood tests are checking rather than using terms such as haematology, coagulation pro-BNP biomarker etc.
9. Replace 'hepatitis, HCV' with 'hepatitis B, hepatitis C' (page 5).
10. Simplify language used in table and remove lines that are not relevant to the participant.
11. On page 7, in relation to CT scanning process, the PIS refers to the radiographer and the technologist. If these are not different roles, please use the one title.
12. Bullet-point observed study drug AEs (pages 13/14). Note that these would usually precede procedural risks, which are all relatively minor. Please also move 'Notable Class Risks' to sit with risks of the study drug.
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16. Delete optional tick boxes for withdrawal of data and GP notification of study participation / abnormal results as these are mandatory for participation.

**Decision**

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1. Please address all outstanding ethical issues, providing the information requested by the Committee.
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4. Please update the data and tissue 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, 14.16&14.17*).

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

## General business

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

|  |  |
| --- | --- |
| **Meeting date:** | 11 April 2023 |
| **Zoom details:** | To be determined |

 The following members tendered apologies for this meeting.

* Dr Devonie Waaka
* Associate Professor Mira Harrison-Woolrych
* Associate Professor Nicola Swain
* Mr Dominic Fitchett
1. **Review of Last Minutes**

The minutes of the previous meeting were agreed and signed by the Chair and Co-ordinator as a true record.

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

The meeting closed at 2.00pm with a karakia.