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| **Committee:** | Northern B Health and Disability Ethics Committee |
| **Meeting date:** | 07 November 2023 |
| **Zoom details:** | 965 0758 9841 |

| **Time** | **Review Reference** | **Project Title** | **Coordinating Investigator** | **Lead Reviewers** |
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| 11:30am - 12:00pm | 2023 FULL 18885 | CRSP-CVD-401: A Study to Evaluate the Safety and Tolerability of CTX320 for the Treatment of Atherosclerotic Cardiovascular Disease (ASCVD) and Calcific Aortic Valve Stenosis (CAVS) | Professor Russell Scott | Kate / Amber |
| 12:00 - 12:30pm | 2023 FULL 18864 | MK-3543-006: Clinical trial of bomedemstat compared to best available therapy in adults with essential thrombocythemia | Dr James Liang | Alice / Leesa |
| 12:30 - 1:00pm | 2023 EXP 19008 | Research priorities for youth mental health and substance use in NZ | Dr Kaaren Mathias | Maakere / Barry |
| 1:00 - 1:30pm | 2023 FULL 18663 | Edwards 12F Sheath Feasibility Study | Dr James Blake | Ewe Leong / Joan |
| **1:30 - 2:00pm** |  | **Break (30 Minutes)** |  |  |
| 2:00 - 2:30pm | 2023 FULL 18311 & 2023 FULL 18313 | A Phase 3, Multi-center, Randomized, Quadruple-masked, Placebo-controlled Study of Batoclimab for the Treatment of Participants with Active Thyroid Eye Disease (TED) & An Open-label Extension Study for Participants who Completed Study IMVT-1401-3201 or Study IMVT-1401-3202 to Assess the Efficacy and Safety of Batoclimab for the Treatment of Thyroid Eye Disease (TED) | Dr Rebecca Stack | Kate / Joan |
| 2:30 - 3:00pm | 2023 FULL 18958 | Improving the dietary intake of residential care facility residents through the fortification of everyday foods. | Dr Karen Munday | Ewe Leong / Barry |
| 3:00 - 3:30pm | 2023 FULL 18809 | A Maori prevalence Study for mate wareware | Dr Makarena Dudley | Maakere / Amber |
| 3:30 - 4:00pm | 2023 FULL 19050 | ULCIP (Ultra Low-Cost Insulin Pump) trial | A/Prof. Martin de Bock | Alice / Leesa |
| **4:00 - 4:20pm** |  | **Break (20 Minutes)** |  |  |
| 4:20 - 4:50pm | 2023 FULL 18823 | The GORE VBX FORWARD Clinical Study | Associate Professor Andrew Holden | Ewe Leong / Barry |
| 4:50 - 5:20pm | 2023 FULL 18873 | A Phase 2/3, Randomized, Open-Label Study of Zanzalintinib (XL092) + Nivolumab-Relatlimab FDC vs Cabozantinib + Nivolumab in Participants with Previously Untreated Advanced or Metastatic RCC | Dr Navin Wewala | Kate / Leesa |
| 5:20 - 5:50pm | 2023 FULL 18950 | Phase 2 Study of Adjuvant V940 and Pembrolizumab in Muscle-invasive Urothelial Carcinoma | Dr Nicola Lawrence | Maakere / Joan |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Ms Kate O’Connor | Lay (Ethical/Moral reasoning) (Chair) | 13/08/2021 | 16/08/2024 | Present |
| Mrs Leesa Russell | Non-Lay (Intervention/Observational Studies) | 13/08/2021 | 16/08/2024 | Present |
| Mr Barry Taylor | Non-Lay (Intervention/Observational Studies) | 13/08/2021 | 16/08/2024 | Present |
| Ms Alice McCarthy | Lay (the Law) | 22/12/2021 | 22/12/2024 | Apologies |
| Ms Joan Pettit | Non-Lay (Intervention Studies) | 08/07/2022 | 08/07/2025 | Present |
| Dr Amber Parry-Strong | Non-Lay (Health/Disability service provision) | 08/07/2022 | 08/07/2025 | Present |
| Mr Ewe Leong Lim | Lay (Consumer/Community perspectives) | 08/07/2022 | 08/07/2025 | Present |
| Ms Maakere Marr | Lay (Consumer/Community perspectives) | 08/07/2022 | 08/07/2025 | Present |

## Welcome

The Chair opened the meeting at 11.00am and welcomed Committee members, noting that apologies had been received from Ms Alice McCarthy.

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 03 October 2023 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **2023 FULL 18885** |
|  | Title: | A Phase 1 Open-label, Multicenter, First-in-human, Ascending Single Dose Study Evaluating the Safety and Tolerability of a Lipid  Nanoparticle Formulation of CRISPR–Guide RNA–Cas9 Nuclease (CTX320) for In Vivo Editing of the Apolipoprotein(a) Gene (LPA) in Subjects with Elevated Lipoprotein(a) and a History of Atherosclerotic Cardiovascular Disease or Calcific Aortic Valve Stenosis |
|  | Principal Investigator: | Professor Russell Scott |
|  | Sponsor: | CRISPR Therapeutics AG |
|  | Clock Start Date: | 26 October 2023 |

Professor Russell Scott, Dr Jane Kerr, Julia O’Sullivan, Saumya Bhatta, and Kayla Malate 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 queried if the 15-year follow-up portion of the study will come as a separate protocol or as an amendment to the current protocol. After discussion, it was clarified that this would be a new protocol with separate review process.
2. The Researchers clarified the streamlined reimbursement schedule can be flexible to participant’s needs.

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 they need continued reassurance about the robustness of the Gene Technology Advisory Committee (GTAC) process and the Researchers could greatly aid the Committee in furthering their understanding of this process. After discussion, the Researchers agreed to send the outcome of the submission via an Amendment submission relating to non-standard conditions, as well as notifying the Secretariat of this submission via email.
2. The Committee queried if the prohibition on donating semen, eggs, blood or organs during study participation in essence will also mean no donation ever again. If there is an indication that this could be the case (given the 15-year follow up), please ensure participants are explicitly told this.
3. The Committee noted that Medpace is stated in the data management plan (DMP) but Castle is stated in the submission form. Please clarify the role of the two groups in the DMP.
4. Page 15 of the participant information sheet doesn’t state what overseas samples will be used for. Given there may be whole genome sequencing and storage for 30 years, this needs to be restricted were appropriate for drug-related uses. The protocol on page 49 states something that looks like future unspecified research (FUR) where it mentions exploratory research as well as in the data management plan in 8.4. Please provide additional clarifications in that section.

**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 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).*

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| **2** | **Ethics ref:** | **2023 FULL 18864** |
|  | Title: | A Phase 3, Randomized, Open-label, Active-Comparator-Controlled Clinical Study to Evaluate the Safety and Efficacy of  Bomedemstat (MK-3543/IMG-7289) versus Best Available Therapy (BAT) in Participants With Essential Thrombocythemia who have  an Inadequate Response to or are Intolerant of Hydroxyurea. |
|  | Principal Investigator: | Dr James Liang |
|  | Sponsor: | Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc. |
|  | Clock Start Date: | 26 October 2023 |

Dr James Liang, Sharon Cheung, Aoibheann Walsh, and Rushdia Zareen Yusuf 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 the mandatory use of devices to complete questionnaires is an equity issue and queried if there are paper options. The Researchers confirmed paper options are available.

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 if the comparator arm contains options for standard of care in New Zealand. The Researcher clarified that all but one is, and the one that isn’t is because it’s not Pharmac funded. If they are randomised to the comparator arm, the investigator has more choices than regular standard of care. The Committee noted that the multiple-drug section and what to do section of the participant information sheet (PIS) is quite confusing for what the options are. A statement early in that section that says ‘some people will stay on their regular treatment or have what treatments are available in hospital, and some people will have the study drug’ will make more sense. This information can be eased into more gently. Titling such as “if you are on the intervention arm” and “if you are in regular care arm”.
2. The Committee asked the Researchers to talk them through the limited screening consent. The Researcher detailed that a lot of people come in with a diagnosis of Essential Thrombocythaemia (ET) that may not be true ET, so this is to ensure correct selection of participants. The Committee replied that this consent form (CF) needs more context and information about what it is about and what they are consenting to. The results too of the biopsy are being kept and analysed for 15 years regardless of whether they have ET and regardless of whether they are in the study. This isn’t screening, this becomes a future unspecified research (FUR) activity. If the Researchers want to keep them for 15 years and use them for any purpose, it needs to be made clear that they are also consenting to FUR whether or not they formally participate in the study, as well as what boundaries to this research there is. The Committee suggested they could borrow from the [HDEC FUR template](https://ethics.health.govt.nz/guides-templates-and-forms/participant-information-sheet-templates/) to inform how this is written up. It is standard that screening is just entry into the study so think about whether the study has folded two things into one. Please also make it clear whether this FUR component, if included, is optional. It is highly recommended that the FUR component is split off this limited screening consent to its own optional FUR PIS/CF.
3. There were two documents with validated scales. Only one document contained a list of the scales, so the Committee are missing those scales. Please provide these.
4. The Committee noted that disability data is not being collected and this is something being asked for from now on to help address inequities. Please investigate how this can be done, even at a site-level.

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

1. Please ensure section 10 includes information on Interferon.

Please provide clarity around whether the biomarker and genetic components are mandatory or not.

1. In the Insurance section remove "The injury was caused by Anagrelide, Busulfan, Interferon and Ruxotilinib" as exception. Compensation must be available for participation injury fand is not related only to investigational product.

**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 Mrs Kate O’Connor and Mrs Leesa Russell.

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| **3** | **Ethics ref:** | **2023 EXP 19008** |
|  | Title: | What are the research priorities for youth mental health and substance use in Aotearoa New Zealand |
|  | Principal Investigator: | Dr Kaaren Mathias |
|  | Sponsor: | University of Canterbury |
|  | Clock Start Date: | 26 October 2023 |

Dr Kaaren Mathias 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 they don’t believe this is health and disability research, however acknowledged the Researcher’s funding situation from HRC and that their available University ethics committee is not HRC approved. Further, there were significant delays caused for the Researcher prior to submission to the HDECs. After discussion, the Researcher agreed with the Committee proceeding with the review to ensure this research can move forward.
2. The Researcher confirmed there is a specialist rainbow group.
3. The Committee noted that if this study wishes to acknowledge the experience and voices of those aged 15 in future, they would accept their ability to consent for themselves. If you want to have a younger group of 12-14, this should come through as an amendment, just ensure that a slightly more simplified participant information sheet (PIS) be provided for them and not pair this younger group with older kids.

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 that if someone wasn’t comfortable with the group setting, whether they have the option of an individual interview. The Researcher confirmed this. The Committee requested this is highlighted in the PIS.
2. Once the survey is developed, please ensure this is submitted to the HDEC as an Amendment for review before use.
3. The Committee requested provision of the focus group guide/rough framework for what will happen during these sessions.
4. The current protocol lacks participant safety plan and how distress will be managed and responded to. Please amend this.

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

1. Please review for page numbers and footers and other minor administrative matters
2. Second paragraph has unfinished sentence.
3. Require contact details for cultural support, please add. Refer to the [HDEC template](https://ethics.health.govt.nz/guides-templates-and-forms/participant-information-sheet-templates/) for an outline.
4. Please remove demographic data collection from the consent form, it is better to separate it for consent obtaining only.
5. Given that some of these groups may have literacy issues, some wording was too adult-like. Please review and amend.

**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 Ms Kate O’Connor and Mr Barry Taylor.

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| **4** | **Ethics ref:** | **2023 FULL 18663** |
|  | Title: | Edwards 12F Sheath Feasibility Study |
|  | Principal Investigator: | Dr James Blake |
|  | Sponsor: | Edwards Lifesciences LLC |
|  | Clock Start Date: | 26 October 2023 |

Dr James Blake and Houda El Banna 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 acknowledged that the valve application sits with the Southern HDEC and it would have been better if it was reviewed with it so there may be extra clarifications required for this committee. After discussion, it was clarified that this application is for the sheath component only, and the valve research can be undertaken without the sheath part. Any information related directly to just the valve component is not covered under this review.

Summary of outstanding ethical issues

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

1. In terms of approach to participant, it currently reads that both parts (the investigational sheath and investigational heart valve) have to be consented to by a participant and is not clear to what they are consenting. There is a separate valve-only study that may recruit from the same pool of potential participants. One approach suggestion from the Committee is that this participant information sheet (PIS) focus on the sheath and make clear that participants are being offered the sheath study because they have already expressed interest in the valve study. As the valve is subject to its own PIS, this approach would achieve a separation of the different parts and clearer to follow. Another approach is rewriting the PIS to state that they have expressed interest in the new valve, and that this study is for the sheath so the studies are related but still separate.
2. If approaching the same eligible group for both studies, participants need to understand the triage of decision making of what study they are enrolled into. Please amend participant documentation to be clearer.
3. The Committee queried the pregnancy/breastfeeding exclusion and why males had to use contraception. The Researcher responded that is related to standard of care and is unlikely to be an issue with these patients. The Committee noted that if this is unrelated to the study, then take it out of the participant information.
4. Please clarify in the protocol what order things are happening in with the valve and sheath studies, both separately and combined. Please dissect the components and wrap it all up together across the documentation. Please note that the valve only study should have good safety data before commencing with a combined valve plus sheath study, since both components are investigational.

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

1. Given that the difference of the sheath to others is just that its smaller, this should be made clearer and whether there are any associated risks.

**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 Mr Ewe Leong Lim and Ms Joan Pettit.

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| **5** | **Ethics ref:** | **2023 FULL 18311** |
|  | Title: | A Phase 3, Multi-center, Randomized, Quadruple-masked, Placebo-controlled Study of Batoclimab for the Treatment of Participants with Active Thyroid Eye Disease (TED) |
|  | Principal Investigator: | Dr Rebecca Stack |
|  | Sponsor: | Syneos Health New Zealand Limited |
|  | Clock Start Date: | 26 October 2023 |

Dr Rebecca Stack, Swamy Chintapatla, and Peter Vue 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 that applications 2023 FULL 18311 & 2023 FULL 18313 are substantially similar as one is the Phase 3 and the other is the open-label extension (OLE). As a result, both were reviewed in the same timeslot as some comments provided for one are related to the other.
2. The Committee confirmed with the Researcher that there was equal opportunity of participation despite the private clinical setting.
3. The Committee noted that C4 of the application form was not answered as expected in response to whether there is disproportionate burden to Māori – answered that they have the same right to participate. The Researchers responded that Thyroid Eye Disease (TED) is incredibly rare in Māori and Pasifika patients and are not more severe if it does occur.
4. The Researchers clarified the nurses do not perform anything else other than providing the injection and collecting some required data in relation to the home visits. There are no assessments.
5. The Committee queried if those that don’t go onto the OLE will be unblinded. The Researchers responded that they will be eventually after all international studies are done.

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 site should make sure that they are using the correct mileage reimbursement rate for the travel policy. The Committee also queried whether its mandatory to use the downloadable app to manage travel bookings reimbursement. The Researcher noted that it is preferred method to use the app but not the only method.
2. The Committee queried if the genetic analysis will be generating something identifiable to the participant. If it is, the risks around this should be outlined. The researcher clarified that it won’t be whole genome sequencing, only a subsection that may indicate how well a participant responds to the drug. The Researcher noted they will confirm that its not identifiable.
3. The Committee requested that it is clarified to the participant that when they finish the study, what medications they can resume.

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

1. The Committee noted that across all PISes, the study is using a hybrid of what HDEC suggest in their template regarding identifiable and coded data and is using an Americanised coverall of “personal information”. This is not clear and requested if it’s possible to revert to the templated ‘my information’ section to ensure it is localised.
2. Please don’t refer to ‘treatment’ as this an experimental study intervention drug.
3. It is not clear what this person would receive as standard care if they do not joined the study. This would be helpful to put in the PIS.
4. Under if something goes wrong, please clarify what industry guidelines will be followed or expand on it. The HDEC recognises that the template statement provided is not fit for use and will be amended in future.
5. It is not clear who would be getting what in the OLE based on what they respond to in Phase 3. Please clarify.
6. Please provide information about alternative treatments on study exit.

**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 Ms Kate O’Connor and Ms Joan Pettit.

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| **6** | **Ethics ref:** | **2023 FULL 18313** |
|  | Title: | An Open-label Extension Study for Participants who Completed Study IMVT-1401-3201 or Study IMVT-1401-3202 to Assess the  Efficacy and Safety of Batoclimab for the Treatment of Thyroid Eye Disease (TED) |
|  | Principal Investigator: | Dr Rebecca Stack |
|  | Sponsor: | Syneos Health New Zealand Limited |
|  | Clock Start Date: | 26 October 2023 |

Dr Rebecca Stack, Swamy Chintapatla, and Peter Vue 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 that applications 2023 FULL 18311 & 2023 FULL 18313 are substantially similar as one is the Phase 3 and the other is the open-label extension (OLE). As a result, both were reviewed in the same timeslot as some comments provided for one are related to the other.
2. The Committee confirmed with the Researcher that there was equal opportunity of participation despite the private clinical setting.
3. The Committee noted that C4 of the application form was not answered as expected in response to whether there is disproportionate burden to Māori – answered that they have the same right to participate. The Researchers responded that Thyroid Eye Disease (TED) is incredibly rare in Māori and Pasifika patients and are not more severe if it does occur.

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 site should make sure that they are using the correct mileage reimbursement rate for the travel policy. The Committee also queried whether its mandatory to use the downloadable app to manage travel bookings reimbursement. The Researcher noted that it is preferred method to use the app but not the only method.

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

1. The Committee noted that across all PISes, the study is using a hybrid of what HDEC suggest in their template regarding identifiable and coded data and is using an Americanised coverall of “personal information”. This is not clear and requested if its possible to revert to the templated ‘my information’ section to ensure it is localised.
2. The Committee noted that it would be helpful if the documents made clear that they are being asked to join because they were in Phase 3.
3. The difference of this OLE study is that individuals will be given it longer than it has been given before. This hasn’t been specifically highlighted or framed as the study not knowing how much this additional time will have an effect on how the drug works.
4. Observational cohort will have a different experience than the active drug cohort. They won’t have to refrain from taking other medications. This should be clear and distinct from those continuing with the active study drug what their obligations and preventions are. Please customise this PIS to that group’s participation.
5. In addition, please state that this group includes all responders, including those on the placebo group that were identified as such.
6. Since the observational group are not receiving the study drug, information about it can be removed from the PIS.

**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 Ms Kate O’Connor and Ms Joan Pettit.

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| **7** | **Ethics ref:** | **2023 FULL 18958** |
|  | Title: | Improving the dietary intake of residential care facility residents through the fortification of everyday foods. |
|  | Principal Investigator: | Dr Karen Munday |
|  | Sponsor: | Fonterra |
|  | Clock Start Date: | 26 October 2023 |

Dr Karen Munday and Charlotte Mawson 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 with the Researcher that the Ryman facility approached Fonterra to help improve the protein content of their resident’s food, which this study has stemmed from. The study product will be a liquid similar to milk that can be used in place of milk for anything as a replacement. Work has been done with healthy participants for internal sensory testing on tolerability. Work has also been done on the resident’s menu so that there is no change to their diet for practicality in adding the supplement to ensure there is no additional burden on the staff.
2. Regarding the conflict of interest (COI), the Researchers are employed by Fonterra testing a Fonterra product which triggers a COI concern. The Committee noted that it is important that this is managed. Given this is a pilot feasibility, it isn’t as big of an issue for this study, but when the Researchers get to testing to see if there is improvement, this needs to be strictly managed with someone independent overseeing data analysis. The Committee recommended thinking about this next step early and ensure a future application discloses this clearly and outlines how this will be managed. The Researchers clarified too that this isn’t the usual approach with them directly running a trial and there will be engagement with independent clinicians.
3. The Researchers confirmed this is a food product that meets food safety standards and will be provided to those who eat the general meal provided to most 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 acknowledged the ethically complex position given the population by nature may not be able to consent or will have variability in their capacity to consent. Enrolling persons who can’t give consent is pretty difficult and has to be done under strict regulations. After discussion, the Committee suggested only including those who have capacity to consent for themselves to avoid any concerns around what looks like proxy-consent as this is not allowed. As this is just likability and tolerability, it would be better to restrict to adults who can give their own fully informed consent to reduce complexity. While it is good to ensure the families are aware of this study, anything involving getting the family to co-sign should be removed from the documentation.
2. The Committee noted locality authorisation is essential for this and should be the village manager.
3. Data management plan (DMP) provided is a brief one-pager. The Committee noted that the [HDEC template](https://ethics.health.govt.nz/guides-templates-and-forms/data-and-tissue-management-plan-templates/) can be used as a guide as currently this lacks information, including what happens to the photos being taken of before and after of food and whether this is identifiable.
4. The Committee queried the process about the photos of the food. The Researchers responded that they have a standard operating procedure (SOP) for this. There is a defined framing for this and will be attached to a number identifier. Purpose of this is to see if they are eating more or eating less. This will be compared to their baseline, and ideally will not see a difference in how much they are eating. The Committee queried how are these photographs being managed and stated that this is level of detail that needs to be worked out in DMP.
5. The Committee noted that insurance expires shortly and an updated one should be provided.
6. The submitted application provide very little description regarding value to Māori and C4 should be fleshed out as there are a lot of issues that could arise from any research that involve Māori. Anything known about nutritional status in older Māori would be good information to provide here.

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

1. Given the short intervention period, it’s unrealistic to claim that the fortified food will improve their nutritional status and health. Make it very clear that the intention is just to see if they like it and keep their volume of food about the same and is as good as this early phase will be able to determine, especially as nutritional status is not being measured.
2. Please describe that the product is available overseas but not here yet which is why this study is being performed.

**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 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).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Mr Ewe Leong Lim and Mr Barry Taylor.

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| **8** | **Ethics ref:** | **2023 FULL 18809** |
|  | Title: | He rapunga hauora mō te matewareware: A prevalence study |
|  | Principal Investigator: | Dr Makarena Dudley |
|  | Sponsor: |  |
|  | Clock Start Date: | 26 October 2023 |

Dr Makarena Dudley and A/Professor Nick Garrett 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 that this study is looking at both prevalence AND experience of living with mate wareware, and this has increased the complexity of the study. The Researchers responded that primarily it’s a prevalence study but it’s important they find out more data around the inequities of Māori with mate wareware while able to have that conversation. It’s an opportunity to collect that data at this time.
2. There is some evidence to suggest that Māori are younger than non-Māori when they are diagnosed. The Committee queried why that age is not lower. The Researchers responded that it was their wish for the age range to be 55 and above, but that includes an enormous increase in people that needed to find. Not within resources to do so. For the next study, the Researchers will recommend the next study captures that under 65 data.

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 provision of the training framework and safety procedures for the field staff to provide assurance that these staff are suitably qualified and aware of what to do if they suspect neglect or abuse, and to manage the complexities of taking consent with persons who present with a range of capacity. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.42-11.44, 11.62 & 11.63*).
2. The Committee raised the supported decision making for consent and queried who is taking it, how is capacity being ascertained, how is the supported decision-making model being worked through. The Researchers responded that Cepstral Spectral Index of Dysphonia (CSID) is being used is like a screen test, so if they ‘screen fail’ for their own consent, they could use that as an indicator that they need further assessment and assistance and will need to seek additional consent from the support person present. Please carefully address the procedures around screening for capacity such as who decides and on what basis, and incorporate this data into the study data plan, as it is likely that any screening will occur prior to consent being given. The Committee noted to consider an alternative approach to include only those who can consent on their own behalf and collect basic demographic information about capacity-screen fails. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.59-7.69*).
3. The Committee noted a requirement to have mandatory support person present during the assessments, and to answer the whānau questionnaires could exclude the socially isolated from study participation. They requested that the Researchers figure out an approach on if staff find someone who truly has no one as they would be needed to be included in the study. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 5.15).*
4. The Committee suggested that scenario planning in detail for different possible outcomes from the first knock would help address the above points, especially the various consent issues. The Committee highlighted these specific scenarios for consideration:
   1. The index participant has received a diagnosis and lacks capacity (or is screened as lacking capacity), even with support. Detail if a waiver of consent to link to health info is being sought, and / or are whānau being asked to answer health questions about them as proxy, and/ or report on the whānau experience of care, and whether the health measures still valid if filled in by a proxy.
   2. The index participant requires the protection of a supported decision-making process but does not have access to suitable people.
   3. The index has capacity but lacks a family or friend to answer the whānau questions.
   4. 2 or more eligible participants reside in the same household, who may (or who may not be) each other's primary caregiver.
   5. Suspected elder abuse and family harm.
   6. Undiagnosed mental health issues or disclosure of suicidality.
5. The Committee queried how Researchers are selecting households. The Researchers are using census data to do some selection of meshblocks where there are a high proportion of Māori and older adults just so we can get a sampling probability. The Committee noted that needs to be made clear in the documentation on how the Researchers reach the door-knocking stage along with what advertisements will be made. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7 & 9.8).*
6. The Committee requested provision of the field staff script at door-knock.
7. In the screening overview of the submission form, please tick relatives and caregivers of consumers to ensure you are largely relying on whānau for this study.
8. The Committee suggested use pronouns in the questionnaires, or koro and kuia, instead of referring to "your kaumatua" all the time.
9. The Committee corrected the use 's' when referring to the plural of any Māori word, e.g., kaumatua's, there is no 's' in the Māori alphabet. Either rephrase the question or use the tohu toa when speaking about more than one kaumatua, e.g., kaumātua.
10. The Committee noted that the Research Office of the University is the sponsor for HDEC purposes. Please obtain this authorisation on the next submission form.
11. The Committee stated that the advertisements in letter boxes should have more generic information about the study as they are currently too specific. Please consider including a contact detail for persons who do not wish to receive an approach by field staff.
12. The Committee noted to consider the potential for stigma, shame or embarrassment that accompanies the concept of caregiver ‘burden’.
13. The Committee noted that whānau filling out the questionnaire as proxy cannot happen unless the member has Enduring Power of Attorney (EPOA) if they are divulging personal information related to their family member’s health or medical care. Please check and confirm the legality of providing health information on behalf of another. They might answer questions related only to their perspective or observations of their family member’s health and behaviour, and this might impact the scientific integrity of data.
14. Please consider the ethical impact of questioning caregiver ‘burden’, particularly in the presence of the index participant.

The Committee requested the following changes to the Participant Information Sheet and Consent Forms (PIS/CFs) *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17)*:

1. Vouchers and kete of kai must be specified as to what it is and who it is for.
2. Data-linkage being optional is not discussed in the PIS or an optional item in the CF. Please amend.
3. Please add that interviews can be in Te Reo or English.
4. “Informant” PIS should be renamed to either whānau or kaiawhina PIS instead.
5. In the kaumatua PIS, please revise section on ethics approval. This is currently unclear who has approved what between HDEC and university.
6. The first part of the Informant PIS looks like it has been copied and pasted from the kaumatua one and should be specific to them. Please make sure they also have a CF.

**Decision**

This application was *declined* by consensus, as the Committee did not consider that the study would meet the ethical standards referenced above. The Committee strongly recommended returning to the Northern B Committee for resubmission.

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| **9** | **Ethics ref:** | **2023 FULL 19050** |
|  | Title: | Clinical trial investigating the efficacy and safety of insulin delivery with a prototype ultra-low-cost insulin pump in adults with type 1  diabetes |
|  | Principal Investigator: | Associate Professor Martin de Bock |
|  | Sponsor: | University of Otago |
|  | Clock Start Date: | 26 October 2023 |

Associate Professor Martin de Bock, Dr Tom Wilkinson, Matt Payne, and Professor Geoff Chase 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.

Dr Amber Parry-Strong declared a potential conflict of interest and the Committee decided to recuse her from discussion.

Summary of resolved ethical issues

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

1. The Researcher clarified with the Committee that there is nothing new in the inside of the pump and is typical of a regular pump – no new mechanism, etc. Nothing patentable, the design is open-access. The benefit to the user and potential user is the increase in accessibility due to decreased cost. Due to the open-access nature of this design being released, while someone could commercially benefit from making it, anyone else could also make it for no cost to users. The software application is also open access for free. The electronic parts were specifically chosen to what generic components are available. The Committee was assured this was not a trial for commercial benefit.
2. The Committee noted the bench testing seemed quite solid, including plans for managing technical and safety failures, particularly around insulin overdose.
3. The Committee also noted that the data management for the study is also adequately detailed.
4. The Committee noted that the peer review made quite a few comments and queried if the Researchers made changes in relation to the peer review. The Researchers responded that the reviewer seemed to be thinking of next-stages, while they are trying to be pragmatic for this current study so they haven’t made any changes as they didn’t think they needed to as investigators. The Committee agreed that the changes didn’t need to be made.
5. The Committee was assured that while all six participants will be tested at once but have adequate staffing to address multiple problems if they occur in a controlled setting.
6. Assured that the clinicians related to participant’s care are not involved in the consenting process.
7. The Committee noted the exclusion of people with disabilities and those with English literacy issues, and queried if there could be support in place. The Researchers responded that given this is a first-in-human study and very small, it’s more of a safety precaution. The Researchers stated they could explain this in future about this criteria, and future studies where they open it up more will address equity of access.

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 provision for their records of information about the software to provide the Committee reassurance around its use and privacy policy. Information on how the device will be disconnected from the internet will also be helpful.

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

1. Further explain why the cost is low. “Cheap” has more connotations.
2. Queried use of pregnancy information given the length of study. This can be significantly reduced or removed.

**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).*

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| **10** | **Ethics ref:** | **2023 FULL 18823** |
|  | Title: | The GORE VBX FORWARD Clinical Study: A Comparison of the GORE® VIABAHN® VBX Balloon Expandable Endoprosthesis to Bare Metal Stenting for Patients with Complex Iliac Occlusive Disease |
|  | Principal Investigator: | Associate Professor Andrew Holden |
|  | Sponsor: | W. L. Gore & Associates, Inc. |
|  | Clock Start Date: | 26 October 2023 |

Associate Professor Andrew Holden and Elleni Takele 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 queried if the two stents being used in the study are in regular use and whether the study is still in equipoise. The covered stent seems to be leaned towards as a preference in the PIS. After discussion, it was that there is no good evidence that one is better than the other so the study is equally balanced, and both stents are in regular use.

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 peer review from a Sponsor employee is not independent enough and does not meet the HDEC requirements for independent scientific peer review.
2. Insurance certificate doesn’t currently name New Zealand as a policy territory, please provide an endorsement addendum of it.

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

1. References to Central HDEC should be amended to Northern B.
2. The Committee queried the restrictions around pregnancy and breastfeeding. The Researcher responded that because this happens in older people, it is unlikely to encounter this. The Committee suggested then that perhaps the risks are overstated, and this information can be provided separately to anyone of child-bearing potential if they are in the 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 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 supply an independent peer review for the current version of the study protocol. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.26).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Mr Ewe Leong Lim and Mr Barry Taylor.

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| **11** | **Ethics ref:** | **2023 FULL 18873** |
|  | Title: | A Phase 2/3, Randomized, Open-Label Study of Zanzalintinib (XL092) Combined with Nivolumab-Relatlimab Fixed-Dose Combination (FDC) versus Cabozantinib combined with Nivolumab in Participants with Previously Untreated Advanced or Metastatic Renal Cell Carcinoma |
|  | Principal Investigator: | Dr Navin Wewala |
|  | Sponsor: | Exelixis Inc |
|  | Clock Start Date: | 26 October 2023 |

Dr Navin Wewala and Susan Newlands 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 for future applications that documents like electronic diary screenshots, training, tote bag design etc, are non-review documents and contribute to overwhelming the application. Please assess for common sense on what should or shouldn’t be included.
2. The Committee queried if the side effects of this study drug is comparable to those used in standard of care (SOC). The Researchers responded that both drugs of control and experimental arms are higher risk than those in SOC in New Zealand, but are higher in efficacy. They are treatments that are not funded in New Zealand but are SOC internationally, and likely would be patient’s choice if available.

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 it’s rare to see a consent for if someone is worsening that they can consent to stay on the study drug. Study documentation, especially the participant information sheet needs more work to adequately explain rationale for this option, and tone and wording for consistency and clarity needs to be reviewed.
2. The Committee noted that proof of indemnity provided expires soon, please provide the updated one.
3. The Committee queried patient recorded outcomes only using a device as a mandatory part of participation. For someone who isn’t tech-savvy, a paper option not being available is an equity of access issue. Either provide a paper option or have the site support use of a device (though notably in self-reported scales, having assistance will affect answers).

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

1. Please state the approval status of the drugs used on page 9.
2. Page 9 also has an overpromise of benefit by stating “reasonable to expect your cancer may improve”. Please review and amend.
3. “Flipping a coin” description for randomisation should be amended.
4. The side effects section is very long in the Main PIS. Two separate columns may make it appear shorter and more condensed. Drugs can also be organised by cohort.
5. Make it clearer which drugs are in what group, the paragraph is currently dense.
6. Alternatives to taking part should be highlighted, particularly what the only funded treatment is or that they can talk to their oncologist about what their options are.

**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 Ms Kate O’Connor and Mrs Leesa Russell.

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| **12** | **Ethics ref:** | **2023 FULL 18950** |
|  | Title: | A Phase 2, Randomized, Double-blind, Placebo- and Active-comparator-controlled Clinical Study of Adjuvant V940 (mRNA-4157) Plus Pembrolizumab Versus Adjuvant Placebo Plus Pembrolizumab in Participants With High-risk Muscle-invasive Urothelial Carcinoma  Post radical Resection |
|  | Principal Investigator: | Dr Nicola Lawrence |
|  | Sponsor: | Merck, Sharp & Dohme (Australia) Pty Ltd (MSD) |
|  | Clock Start Date: | 26 October 2023 |

Dr Nicola Lawrence and Daphne Mason 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 Researchers confirmed that even if participants are assigned to the control arm, they receiving better than standard of care (SOC).

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 they need continued reassurance about the robustness of the Gene Technology Advisory Committee (GTAC) process and the Researchers could greatly aid the Committee in furthering their understanding of this process. After discussion, the Researchers agreed to send the outcome of the submission via an Amendment submission relating to non-standard conditions, as well as notifying the Secretariat of this submission via email.

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

1. Please ensure the PIS used is localised to the site as reimbursement templated statements were still included.
2. There is a page 3 statement that says “your tumour tissue sample may be used to develop tests… to help people with cancer”. This statement is a bit loose and very general as if its future unspecified use, please remove as it’s explained later in more detail.
3. Refer to the study drug as study medicine or study drug, not treatment.

**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).*

## General business

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

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| **Meeting date:** | 05 December 2023 |
| **Zoom details:** | To be determined |

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 5.50pm