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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 15 February 2022 |
| **Zoom details:** | https://mohnz.zoom.us/j/96507589841 |

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| **Time** | **Review Reference** | **Project Title** | **Coordinating Investigator** | **Assigned Lead Reviewers** |
| 12:30pm – 1:00pm | 2021 FULL 11916 | Delta-Max Trial | Professor  Jamie Sleigh | Dr Kate Parker &  Ms Catherine  Garvey |
|  |  | *Break (30 minutes)* |  |  |
| 1:30pm – 2:00pm | 2022 FULL 11760 | M20-178 (TRANSFORM-2) Myelofibrosis: Phase 3  Study of Navitoclax Plus Ruxolitinib Versus Best  Available Therapy | Dr James  Liang | Dr Sotera  Catapang & Dr  Leonie Walker |
| 2:00pm – 2:30pm | 2022 FULL 12039 | Nutrition status in childhood cancer | Dr Amy  Lovell | Ms Amy Henry  & Ms Catherine  Garvey |
|  |  | *Break (20 minutes)* |  |  |
| 2:50pm – 3:20pm | 2022 FULL 12069 | A Study to Assess the Safety, Effects and How the Body  Processes a New Drug, NT-0249 in Healthy Adults | Dr Chris  Wynne | Dr Kate Parker &  Mr Jonathan  Darby |
| 3:20pm – 3:50pm | 2022 FULL 11309 | PRoMPT Bolus; SENTINEL sub-study | Professor  Stuart Dalziel | Dr Karen  Bartholomew &  Ms Catherine  Garvey |
| 3:50pm – 4:20pm | 2022 FULL 11840 | Allo Allo Study | Assoc Prof  Yoram Barak | Ms Jade Scott &  Dr Leonie Walker |
| 4:20pm – 4:50pm | 2022 FULL 11818 | RESTORE-MI Trial | Professor  Harvey  Douglas  White | Ms Amy Henry  & Mr Jonathan  Darby |
|  |  | *Break (10 minutes)* |  |  |
| 5:00pm – 5:30pm | 2022 FULL 11612 | Intraosseous Regional Administration of Diclofenac  (IRAD) in Primary TKA Study | Mr Simon  Young | Dr Leonie Walker |
| 5:30pm – 6:00pm | 2022 FULL 12019 | A study to assess differing doses of IMU-856 in healthy  volunteers and patients with celiac disease | Professor  Richard  Stubbs | Dr Kate Parker & Ms Catherine Garvey |
| 6:00pm – 6:30pm | 2022 FULL 11715 | A cohort study to evaluate the effect of ADF in adults  with T2DM | Dr. Pedram  Zawarreza | Dr Sotera  Catapang & Mr  Jonathan Darby |
| 6:30pm – 7:00pm | 2022 FULL 12051 | Phase 2 Study Investigating the Efficacy and Safety of  BGE-117 in Moderately to Severely Anaemic Older  Individuals After Major Hip Surgery | Dr John  Currie | Ms Amy Henry  & Dr Leonie  Walker |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Ms Catherine Garvey | Lay | 11 August 2021 | 11 August 2024 | Present |
| Ms Jade Scott | Non-Lay | 15 August 2021 | 15 August 2024 | Present |
| Dr Andrea Forde | Non-Lay | December 2021 | December 2024 | Apologies |
| Dr Leonie Walker | Lay | 13 August 2021 | 13 August 2024 | Present |
| Mr Jonathan Darby | Lay | 13 August 2021 | 13 August 2024 | Present |
| Dr Kate Parker | Non-Lay | 11 November 2015 | 11 February 2023 | Present |
| Ms Amy Henry | Non-Lay | 13 August 2021 | 16 August 2024 | Present |
| Dr Sotera Catapang | Non-lay | 11 February 2020 | 11 February 2023 | Present |

## Welcome

The Chair opened the meeting at 12pm and welcomed Committee members, noting that apologies had been received from Dr Andrea Ford.

The Chair noted that it would be necessary to co-opt members of other HDECs in accordance with the Standard Operating Procedures. Ms Amy Henry confirmed eligibility and was co-opted by the Chair as members 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 16th of November 2021 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **2021 FULL 11916** |
|  | Title: | Delta-Max Trial |
|  | Principal Investigator: | Professor Jamie Sleigh |
|  | Sponsor: | Waikato District Health Board |
|  | Clock Start Date: | 3rd February 2022 |

Professor Jamie Sleigh and Mr Jono Termaat 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 Study

1. This study will lay the groundwork for the future possible development of a more accurate depth of anaesthesia monitoring system. The improvement in health outcomes will be better control of anaesthetic delivered and greater assurance of depth of anaesthesia for the primary anaesthetist.

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 for clarification on how participants will be recruited for the trial. The Researcher explained that possible Participants would be screened one week prior to the trial, and first contact would be made with the participants anaesthetist to ensure they felt their patient was a good fit and it was safe for them to take part in the trial. Contact would then be made with the participant via telephone to discuss the possibility of taking part in the trial and address any questions. Once participants have indicated their interest in taking part in the trial, the participant information sheet (PIS) would be sent via email. Any further questions and final confirmation would be discussed in person immediately prior to the 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 requested for Waikato Hospitalto be added to the documentation as a site.
2. The Committee asked for the Derriford lab to be added to the Data and Tissue Management Plan.
3. The Committee requested that current CI indemnity documentation be uploaded.

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

1. Please reword or explain ‘delta waves’ in lay language.

**Decision**

This application was *approved with Non-Standard Conditions* 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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| **2** | **Ethics ref:** | **2022 FULL 11760** |
|  | Title: | M20-178 (TRANSFORM-2) Myelofibrosis: Phase 3  Study of Navitoclax Plus Ruxolitinib Versus Best  Available Therapy |
|  | Principal Investigator: | Dr James Liang |
|  | Sponsor: | AbbVie Pty Ltd |
|  | Clock Start Date: | 3rd February 2022 |

Dr James Liang, Shilpa Jain and Megan Bower 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 Study

1. The clinical hypothesis is that Navitoclax, when combined with ruxolitinib in relapsed/refractory participants, is reasonably likely to result in higher and more durable spleen reduction, greater reductions in disease symptoms, reversal of bone marrow fibrosis, and more allelic burden reductions than the current standard therapies.

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 for clarification on the consenting process (timeframes, opportunities to review and discuss with others, etc). The Researcher explained that the consenting process will be dependent on the referral source. However, generally clinicians will refer based on patient relapse on ruxolitinib and whether they fit the inclusion criteria for the trial. Once identified, a member of the research team will make contact and explain the trial. The participant then has time to consider prior to consenting to the study.
2. The Committee asked for clarification on the treatment length should the medicine be proven beneficial to the participants. The Researcher explained that the study drug will continue to be supplied while available and while the participant continues to have clinical benefit, until discontinuation by the PI or the participant voluntarily withdraws.
3. The Committee queried the approach the research team will take regarding follow-up with participants, particularly in cases where a participant may have died. The Researcher explained that they will have access to registries which will have information on the status of the participant.
4. The Committee asked for more information on what Covid-19 processes would be followed and whether these would impact the study. The Researcher explained that they do not anticipate any substantial impacts to the study process and other similar trials overseas which were conducted during the Omicron wave did not indicate increased risk.
5. The Committee asked for clarification on the protocol referring to the possibility of a worsening or enhancement of the thrombocythemia as a result of combining drugs, and what precautionary measures will take place if required. The Researcher explained that the drug combination is known to result in low platelet count, and so many procedures are already in place. For example, the operator conducting the procedure will always check the blood test results to check platelet levels. If the platelet levels are low, they will give a platelet transfusion. Other interventions will take place as required, such as introducing medications to manage any side effects.

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 when will be the primary endpoint SVR35 will be conducted. The Researcher explained that this would be at week 24 of the study. The Committee requested that this is clarified.

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

1. Please specify which biological samples (blood, urine, stool, tissue) are analysed.
2. Please specify the tests to be handled for each overseas laboratory.
3. Please specify the frequency and amount of blood per peripheral blood testing related to low platelet count level of the participants.
4. Please specify in lay terms the timing of intake of Navitoclax since food increases the bioavailability of the drug.
5. Please clarify when the survey questionnaires be conducted and take into consideration the health condition of the participants and possible side effects of the drugs.
6. Please mention the risk of stress and any support that will be available.
7. Please clarify on withdrawing a participant from the study depending on how they are reacting to the drug.
8. Please remove the statement on contacting relatives if the participant has passed away.

**Decision**

This application was *approved with Non-Standard Conditions* 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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| **3** | **Ethics ref:** | **2022 FULL 12039** |
|  | Title: | Nutrition status in childhood cancer |
|  | Principal Investigator: | Dr Amy Lovell |
|  | Sponsor: |  |
|  | Clock Start Date: | 3rd February 2022 |

Dr Amy Lovell 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 Study

1. The study aims to determine the feasibility of collecting biological samples and clinical data to determine the prevalence of micronutrient abnormalities and changes in anthropometry and body composition in a prospective sample of newly diagnosed child cancer patients.

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 the age range of participants was 18 years and younger, as while a childhood diagnosis of cancer is classified below 15 years, Starship Hospital treats patients up to 18 years old.
2. The Committee clarified the quality of life and depression scale would be undertaken by participants whilst in the inpatient or overnight stay setting. There would be follow up of any concerns with the psychological staff on the oncology ward at Starship.

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 requests that the documentation be amended to detail that participants are 18 years and younger.
2. The Committee requested the following changes to the Data Management Plan:
   1. Please update the consent and assent statements to reflect changes to the Consent Forms (CF) and Assent Forms (AF).
   2. Please amend to include a statement addressing the participants right to access and correct data.
   3. Please review for legislature references that are out of date.

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

1. The Committee suggests removing set age bands on information and consent/assent forms and amend forms to be provided as per the competency of the young person not necessarily based on their age. This may be achieved as having different levels of detail in these forms with more diagrams for explanation of the protocol. Please see the National Ethics Standards 6.22 to this effect.
2. Review further for lay language given the comment on removing age bands.
3. Please use the terms “parent or guardian” when mentioning consent in all forms.
4. Please amend to include a statement concerning the future unspecified research (FUR) and make this optional, with a separate PISCF.
5. Please include the risks as mentioned in the application form (section E1).
6. Please explain the Emotional thermometer and the Quality-of-Life assessment.
7. Please note that all health data must be kept for 10 years after the last child turns 16. Please amend accordingly.
8. Please include a statement or inform of processes in place to inform participants of the results or findings of the study.
9. Please ensure the references in the documentation are to the current Privacy Act 2020.

**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 Ms Catherine Garvey and Ms Amy Henry.

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| **4** | **Ethics ref:** | **2022 FULL 12069** |
|  | Title: | A Study to Assess the Safety, Effects and How the Body  Processes a New Drug, NT-0249 in Healthy Adults |
|  | Principal Investigator: | Dr Chris Wynne |
|  | Sponsor: | NodThera Ltd & Novotech NZ Ltd |
|  | Clock Start Date: | 3rd February 2022 |

Dr Chris Wynne and Sharmin Bala 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 Study

1. The study aims to evaluate the safety/tolerability, pharmacokinetics and pharmacodynamics of single and multiple ascending doses of NT-0249 in healthy volunteers.

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 the inability of participants to access their information and data from the application, this was not reflected in the participant information sheet (PIS) and the Committee noted that participants have a right to do so.
2. The Committee clarified that the insurance amount of $10 million dollars may not be sufficient, and the researcher will review this.

Summary of outstanding ethical issues

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

1. The Committee requested that current evidence of the CI’s indemnity be provided.
2. The Committee requested section F9 be answered correctly in the application concerning future unspecified research (FUR). Currently this is not correct.
3. The Committee requests advertisements be amended to inform participants of the restriction to smoking over the study period.
4. The Committee requested the following changes to the Data Management Plan:
   1. Please include a section regarding optional genetic testing, specifically the incidental finding of significant genetic results, and a plan for should these results be shared.
   2. Please amend by reference to the HDEC template the statement on privacy breach to reflect the way in which breaches will be reported to HDECs, the Privacy Commissioner and Participants, and under which circumstances and when this may occur. The Committee noted that reporting to participants should not be restricted to a notifiable breach.
5. The Committee noted that the inclusion and exclusion criteria in the Protocol does not require exclusion of participants who have not received approved COVID-19 vaccinations; rather, this is a site requirement. The PIS needs to be amended to reflect this.

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

1. Please remove ‘healthy’ from ‘healthy human volunteers’ from the black box warning, this is a first-in-human trial not a first in a healthy human trial.
2. Please correct the information on the chance of receiving active drug (6/8, not 5/6).
3. Please include a statement regarding the availability of dietary options for participant stay.
4. Please remove contact of a general practitioner from the optional section of the consent form. This should be mandatory.
5. Please specify the locations that the samples and data may be sent and detail specifically the steps in place to prevent privacy breach.
6. Please remove reference to COVID-19 vaccination as an inclusion criterion. Advice as to the site’s requirements for vaccination may be included.
7. In the optional genetic research PIS, please remove part about GP being contacted about abnormal results from the CF
8. Please also emphasise the risks of data privacy – particularly if you are saying the samples may be sent to other countries as yet unknown.

**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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| **5** | **Ethics ref:** | **2022 FULL 11309** |
|  | Title: | PRoMPT Bolus; SENTINEL sub-study |
|  | Principal Investigator: | Professor Stuart Dalziel |
|  | Sponsor: |  |
|  | Clock Start Date: | 3rd February 2022 |

Professor Stuart Dalziel and Dr Eunicia Tan 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 Study

1. The study aims to determine if fluid resuscitation with balanced fluids will improve clinical outcomes, including a decrease in incidence of major adverse kidney events within 30 days (MAKE30), compared to 0.9% saline in children with septic shock.

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 there would be enrolment of roughly 12 to 24 participants across the two sites.
2. The Committee clarified that enrolment needs to occur in a time-critical manner and as such in many cases there would be no proper opportunity to obtain informed consent.
3. The Committee clarified the consultation with Māori groups was undertaken to ensure that approach of whānau and tamariki would be appropriate.
4. The Committee clarified that the treating clinician would be able to determine which fluid to use of the two available options in NZ, whould there be a clinical reason to prefer one over the other.
5. The Committee clarified the exclusion of those in child-protective services was due to the difficulties associated with obtaining informed consent from a parent or guardian on or during admission.
6. The Committee clarified that due the National Instituites of Health (NIH) sponsorship the future research is not optional.
7. The Committee clarified that any decision on notifying whānau of a deceased participant about the study (when they were enrolled prior to an ability to obtain informed consent) will be carried out on a case by case basis.

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 an independent New Zealand peer review.
2. The Committee requested details on the register that would be developed as part of the sentinel sub-study, including that participant in the registry would occur with informed consent. Information on the data storage, location and safety measures ensuring the security of data is required. Please refer to the NEAC Standards guidance on databanks/registries.
3. The Committee requested the researchers to provide copies of the questionnaires to be used (appendix 2 to the Protocol).
4. The Committee requested that the researcher consider whether it was appropriate to include as a possible benefit the benefit of study findings should the participant experience sepsis in future.

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

1. Please review for language to reflect that some individuals may have already been involved
2. Please include the number of New Zealand participants
3. Please review the section on the potential benefit concerning the risk of future likelihood of sepsis and potential outcome to prevent undue concern of consenting parties.
4. Please review protocols pertaining to informing of participant families of the trial in the event of potential death of participants.
5. Please make it clear that inclusion into future research is not optional.
6. Please include a statement for a participant’s right to access and correct their data, and how the researchers will manage any data privacy breach. Please see the [HDEC template for a Data Management Plan](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/data-only-management-template-oct2020.docx) for guidance.
7. Please include a statement addressing and informing participants of the right to access and correct their data.

**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 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 Ms Amy Henry and Ms Catherine Garvey.

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| **6** | **Ethics ref:** | **2022 FULL 11840** |
|  | Title: | Allo Allo Study |
|  | Principal Investigator: | Assoc Prof Yoram Barak |
|  | Sponsor: | The Kinsman Foundation |
|  | Clock Start Date: | 3rd February 2022 |

Associate Professor Yoram Barak and Professor Paul Glue 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 Study

1. The study aims to measure plasma allopregnanolone (ALLO) concentrations between 0-48 hours after 8-hourly dosing with extended-release progesterone capsules, and to assess the safety and tolerability of extended-release progesterone capsules in healthy volunteers to confirm the model seen in the Phase 1 study for the treatment of post-partum depression (PPD).

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 participants would be individuals that did not have endogenous progesterone in their system. This would include men and post-menopausal women.
2. The Committee clarified that the sedative effect of the drug is minor and not a threat to the health of participants.
3. The Committee clarified the definition of ‘normal’ social use of alcohol as one or two standard drinks during the study period

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 Researcher acknowledged to the Committee that they must complete analysis of phase 1 prior to commencing phase 2 of the study.
2. The Committee requested more detail in the protocol as to the consent process.
3. The Committee requested that the advertisement include information of the exclusion criteria and the time that will be required for participation.
4. The Committee requested that the exclusion criteria be more specific in terms of the exclusion of individuals with liver dysfunction, venous thrombosis etc. as per the contraindications described in the progesterone data sheet.
5. The Committee stated more information around data management is required than what is available in the study documentation to satisfy the Committee that privacy and confidentiality is protected and that Standard 12.15a is met. Use of the HDEC template from the [HDEC website](https://ethics.health.govt.nz/guides-templates-and-forms/) is not mandatory but is encouraged to be adapted or used as a guide/starting point.
6. The Committee recommended the inclusion of a plan for additional recruitment in the event of a missed dose.
7. The Committee queried the peer review provided by Dr Huthwaite and the note made therein of lack of security detail that had not been reflected in the protocol. Please address this.
8. The Committee requested consideration of Māori cultural values and concerns in the study following review by the Māori consultation being sought.

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

1. Please amend the amount of blood drawn to be in teaspoons or tablespoons where appropriate.
2. Please specify how vital the midnight dosage timeframe is and the management of this situation may need to be developed. Include information for participants that they will receive text reminders for dosing.
3. Please include all adverse events and their incidence found in the data sheet as a ratio of likelihood.
4. Please consider inclusion of definitions around alcohol drinking and the extent this should be restricted.
5. Please include the contact details of a Māori support.
6. Please state for participants that there is no approval of progesterone for this purpose or in males.

**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 supply a more detailed data management plan to ensure the safety and integrity of participant data *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Dr Leonie Walker and Ms Jade Scott.

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| **7** | **Ethics ref:** | **2022 FULL 11818** |
|  | Title: | RESTORE-MI Trial |
|  | Principal Investigator: | Professor Harvey Douglas White |
|  | Sponsor: | The University of Sydney. NHMRC Clinical Trials Centre & Green Lane Coordinating Centre Ltd |
|  | Clock Start Date: | 3rd February 2022 |

Sarah Preston and Caroline Alsweiler 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 Study

1. The results of this study will improve understanding into the pathogenesis of myocardial infarction and its relationship with microcirculatory dysfunction. The results of this study may lead to a novel therapeutic approach that could improve the outcomes of patients with myocardial infarction.

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 for clarification on who will initially be approaching potential participants. The Researcher stated this would be either the research coordinator or an investigator who, in some cases, may be performing the Percutaneous Coronary Intervention (PCI) procedure in the lab on the day. The research team will be present on the day, will be notified when a potential participant is approaching the emergency department (ED), and will then approach that participant in ED.
2. The Committee asked whether potential participants would be premedicated. The Researcher confirmed potential participants would be premedicated with morphine when being spoken to, as is standard care. The clinician will assess the dosage and status of the potential participant on the day to determine whether they are fit to provide consent.
3. The Committee asked whether the short version of the Participant Information Sheet and Consent Form (PIS/CF) will be the standard PIS/CF given to potential participants before the procedure. The Researcher confirmed that the shorter form will be used to gain participants’ consent before the procedure, then the larger PIS/CF would be given to participants following the procedure. The longer PIS/CF may be used before the procedure if there are any delays on entering the catheterization lab as there can be delays up to an hour, in which case, participants would be given the longer PISCF as they will have more time to read it.
4. The Committee asked whether this procedure adds time or risk to patients. The Researcher responded that it does add some time to the procedure but that it gives the clinician a better prognostic value of how well the patient is likely to do following their ST-segment elevation myocardial infarction (STEMI).
5. The Committee asked whether the Index of Microcirculatory Resistance (IMR) tests were part of standard care or if there are specific to this study. The Researcher stated that it is a procedure that many clinicians are using when they perceive there is a need for it, however, it is not a part of standard procedure.

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 asked about the role of GenenTech in this study and requested further clarification over what data GenenTech will receive and what them reviewing any publications would mean. Please also ensure GenenTech is not receiving any raw data, only deidentified data.
2. Please reconsider the exclusion criteria regarding those with serious medical or psychiatric conditions. Should this be changed, please consider supported decision-making methods to support people who have a condition that might make participating in the trial challenging. This could involve providing information in a way that’s suitable for the person and making information more accessible.
3. Please provide a more detailed explanation on what participants’ data will be stored for the registry, how and where it will be stored, and who is responsible for it either in the protocol or in an appendix specific to New Zealand if you are unable to include this in the protocol. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.40 – 12.44).*
4. The Committee requested the following changes to the data management plan (DMP):
5. Please include a section around breaches of privacy and describe any actions that would be taken in the event of a breach using the template from the [HDEC website](https://ethics.health.govt.nz/guides-templates-and-forms/data-and-tissue-management-plan-templates/) as a guide.
6. Please include a cultural section using the template from the [HDEC website](https://ethics.health.govt.nz/guides-templates-and-forms/data-and-tissue-management-plan-templates/) as a guide.
7. Please state what follow-up data will be collected for any participants who withdraw from the study.

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

1. Please reword the long form PISCF so it also makes sense for those who have seen the short version and undergone the procedure.
2. Please include information on any blood samples being sent overseas.
3. Please include a separate optional ‘Future Unspecified Research’ (FUR) PIS.
4. Please include a cultural statement, using the template on the [HDEC website](https://ethics.health.govt.nz/guides-templates-and-forms/participant-information-sheet-templates/) as a guide. If no karakia will be available, please state this.
5. Please include a brief description of genetic testing and what this means in lay terms.
6. Please state what follow-up data will be collected for any participants who withdraw from the study.
7. Please include a section in the CF where participants can choose to consent whether they will allow information being gathered on their family.
8. Please include information on any procedures that deviate from standard care.

**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 Jonathan Darby & Ms Amy Henry.

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| **8** | **Ethics ref:** | **2022 FULL 11612** |
|  | Title: | Intraosseous Regional Administration of Diclofenac  (IRAD) in Primary TKA Study |
|  | Principal Investigator: | Mr Simon Young |
|  | Sponsor: |  |
|  | Clock Start Date: | 3rd February 2022 |

Simon Young and Jian-Sen Ng 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 Study

1. The study builds on existing knowledge of intraosseous regional administration and its potential applications, which is a growing area in orthopaedic surgery. Publishing evidence to demonstrate the superiority of IORA of analgesia may lead to changes in routine practice in order to minimise postoperative pain. Improved pain relief using this technique should theoretically lead to reduced systemic opioid consumption and therefore a reduction in side effects from opioids. Overall using this technique and providing improved pain relief should lead to overall better patient outcomes/quality of life following total knee joint replacements with improved recovery after their operation.

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 pain forms and if they are standard or not. The Researcher explained that most of them are standard and protocolized, the main one being used, the “analogue visual scale” is used across different studies and not just pain as it is a relevant scale.
2. The Committee asked about the other data being collected and if that Is coming directly from the medical records of the participants and if any other data would be collected. The Researchers explained that no other data would be collected.
3. The Committee asked if the participants’ family would be able to assist the participants when filling out the questionnaires. The Researchers explained that nurses would assist in the beginning so the participant can do it by themselves later as well.

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 for the font to be larger in the patient outcome form, use of small font may be difficult to read for some participants.

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

1. Please provide Māori contact details.
2. Please clarify include more information on the sponsor and any data that is being shared with them.
3. Please include an option for participants to consent to future unspecified research (FUR).
4. Please remove the reference to a sponsor receiving information under the security and storage heading.
5. Please include the saline (placebos) when defining the two treatment arms to ensure blinding.

**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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| **9** | **Ethics ref:** | **2022 FULL 12019** |
|  | Title: | A study to assess differing doses of IMU-856 in healthy  volunteers and patients with celiac disease |
|  | Principal Investigator: | Professor Richard Stubbs |
|  | Sponsor: | Avance Clinical |
|  | Clock Start Date: | 3rd February 2022 |

Professor Richard Stubbs and Ms Amelia Bohle 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 Study

1. The Primary Study Objective is to assess the safety and tolerability of IMU-856 when administered as a 28-day repeat dose in patients with Celiac Disease (PART C). The Secondary Study Objectives are: To assess the pharmacokinetics (PK) and trough plasma concentration levels of IMU-856 following administration of a 28-day repeat dose in patients with Celiac Disease. To assess the safety and tolerability of administrating IMU-856 in a 28-day repeat dose schedule in patients with CelD during periods of gluten-free diet (GFD) and gluten challenge. To investigate the effect of IMU-856 on the gastrointestinal architecture and inflammation in patients with CelD during periods of GFD and gluten challenge.

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 whether Standing Committee on Therapeutic Trials (SCOTT) had approved the study. The Researchers explained that the study is currently under review from SCOTT.
2. The Committee asked the Researchers if they have any commercial interest in the study as they are a director for P3 research. The Researcher explained they have no commercial interest.
3. The Committee asked how they are going to select people who do not have severe symptoms in response to a gluten challenge, and how the researcher is going to know this. The Researchers explained that they will talk to the potential participants about the strict diet and how they are affected if they have gluten, and if they ever get violently unwell. Those who are expected to have severe symptoms will not be enrolled.
4. The Committee asked what will happen if a participant has a bad reaction to gluten while on the study. The Researcher explained that they anticipated if a participant was to have a severe reaction this would happen on the participants first dose and would be withdrawn from the study for their safety.
5. The Committee asked if any of the tissue is going overseas. The Researcher explained that it is going overseas, and the samples being sent to the laboratories are mentioned in the application submitted.
6. The Committee asked about the gluten challenge and if someone was ordinarily symptomatic because they are inadvertently exposed to gluten from their diet, if there is any medication to alleviate symptoms for those people. The Researcher explained that if someone has bad enough symptoms it will be stomach pain & vomiting and they will assist in alleviating those symptoms.
7. The Committee clarified that participants would receive reimbursement for their time to a reasonable level as well as travel expenses.

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 asked for clarification on how participants will be reimbursed for this trial.
2. The Committee asked for the standard reimbursement to cover costs as providing travel receipts can be difficult for participants.
3. The Committee asked the Researchers to remove the following from the application form “all participants will have access to the study drug after the study”
4. Please include in the protocol how you will manage participants who are ordinarily symptomatic because they are inadvertently exposed to gluten from their diet.

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

1. Please amend the risks related to the study section to be formatted to be more readable.
2. Please remove “also called AIDS” in reference to HIV.
3. Please advise participants if karakia will be available at time of disposal.
4. Please amend the gluten challenge daily for 14 days by explaining it in greater detail and give better reasoning when explaining the anticipated recovery from the effects of this in coeliac patients who ordinarily maintain a gluten free diet.
5. Please explain what ‘sentinel dosing’ is.
6. Please include the laboratories being used for the screening tests.
7. Please include a statement that people who experience severe symptoms when accidentally exposed to gluten will not be included in the trial.
8. Please include information on the possibility of incidental findings during biopsy and what will happen if any incidental findings occur .
9. Please include that potential participants and participants will be questioned about their mood or mental health and what will happen if someone shows distress during the study.
10. Please inform participants that they will be able to access results of genetic testing.
11. Please amend the statement You must confirm to the investigator that, to the best of your knowledge, you are not pregnant now, and that you do not intend to become pregnant during the study.” To reflect that a pregnancy test will be conducted before a participant is enrolled.

**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 Dr Kate Parker and Ms Catherine Garvey.

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| **10** | **Ethics ref:** | **2022 FULL 11715** |
|  | Title: | A cohort study to evaluate the effect of ADF in adults with T2DM |
|  | Principal Investigator: | Dr Pedram Zawarreza |
|  | Sponsor: | University of Centerbury |
|  | Clock Start Date: | 3rd February 2022 |

Dr Pedram Zawarreza, Dist. Prof. Geoff Chase & Ms. Jennifer Ormsbeepresent 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 Study

1. The aim of this study it to determine if metabolic changes in people with T2DM can be attained through free-living fasting. The objective of this study is to determine if Alternate Day Fasting (ADF) can improve insulin sensitivity and insulin secretion in people with T2DM and to determine if there are changes in non-insulin mediated glucose uptake (NIMGU) and insulin mediated glucose uptake (IMGU). Oxidative stress will also be measured at the start and end of the trial to determine if oxidative stress indicators have changed due to the fasting regime.

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 what the Dynamic Insulin Sensitivity and Secretion Test (DISST) involves.
2. The Committee enquired about who will be conducting the DISST tests. The Researcher explained that clinicians who are experienced with the DISST procedure will be involved in the study.
3. The Committee asked for clarification on the requirements of the alternate day fasting, such as specific food restrictions. The Researcher stated that there are no restrictions to what can be consumed during the study, however participants are asked to fast for 14 hours before the DISST tests. Participants are asked to supply a food diary to gauge how eating patterns may have changed during the fasting periods.
4. The Committee asked for more information on whether there would be any adjustments to the insulin being administered to the participant depending on how they are reacting to the study. The Researcher explained that each participant will have an implanted Continuous Glucose Monitor (CGM) which will feed back data to the Researchers. Should there be a change in insulin levels that requires action, the study clinician will intervene and adjust the insulin as necessary.
5. The Committee asked for information on how the Researchers would manage the possibility of hypoglycaemia among participants at home. The Researcher explained that the participants will be given guidelines on how to manage any non-threatening symptoms of hypoglycaemia at home, such as increasing sugar intake. The Researchers will be closely monitoring sugar levels through the CGM and provide advice accordingly.
6. The Committee asked for clarification on the outcome measures of the study. The possible measurable outcomes of the study will be whether patients will be able to come off insulin or their insulin levels have reduced during the study period. If these outcomes occur, a further DISST test will be administered to determine what has changed for the participant. If this is the case, the Researcher would look to future trials with a larger control group over a longer period of time.
7. The Committee asked what would happen to participants who did not comply with the fasting guidelines. The Researcher explained that they would attempt to mitigate the risk of participants breaking the fast through supplying a health coach to set guidelines before and during the study. The clinician will also have access to the CGM readings and approach the participant if there are any variables indicating non-compliance.
8. The Committee asked about the small control group (8-12 participants) and whether any non-compliant parties would be replaced during the study. The Researcher explained that if there are non-compliance (i.e. over half the control group) this is an indication that fasting is not a feasible treatment and this would inform the outcome of the study.
9. The Committee asked for clarification on whether participants or a clinician would be applying the CGM device. The Researcher explained that the CGM would be installed by the trial clinician and that the control group will likely have used CGMs in the past and are familiar with the procedure.
10. The Committee asked for more information on the active recruitment of Māori and Pacifika participants. The Researcher explained that they will ensure that there is equitable access to the study for Māori and Pasifika, however they will not actively seek out Māori and Pasifika participants due to the small control group size.

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 asked that the research team ensure there is a third party (i.e., not a clinician involved in the participants care) who can explain the study to the participant to avoid any conflicts of interest.

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

1. Please provide more information on the CGM and the DISST procedure and be sure to outline the possible risks involved with these devices and procedures.
2. Please provide more information on the clinician’s role in monitoring, availability and the insulin protocol the clinician will be following to ensure participants are safe throughout the study.
3. Please include cultural considerations.
4. Please provide clarity on what can be consumed during the study and define what fasting entails for the purpose of the study.
5. Please provide further information on what happens if the fasting guidelines are not followed correctly.
6. Please include information so it is clear to participants that they will be informed if there are abnormal results.
7. Please ensure that participants GP or healthcare providers are informed if there are any changes to insulin levels.
8. Please include further information on the inclusion criteria for pregnant participants and include a contraceptive statement if necessary.
9. Please remove the word “inducement”.
10. Please include all details about the sites used for 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).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Dr Sotera Catapang and Mr Jonathan Darby.

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| **11** | **Ethics ref:** | **2022 FULL 12051** |
|  | Title: | Phase 2 Study Investigating the Efficacy and Safety of  BGE-117 in Moderately to Severely Anaemic Older  Individuals After Major Hip Surgery |
|  | Principal Investigator: | Dr John Currie |
|  | Sponsor: | BioAge Labs Inc & Research Associates Ltd |
|  | Clock Start Date: | 3rd February 2022 |

Dr John Currie 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 Study

1. The primary objective is to examine the efficacy of 3 dose levels of the hypoxia inducible factor-prolyl hydroxylase inhibitor (HIF-PHI) BGE-117 in improving the time to hemoglobin recovery, when administered with oral iron for up to 12 weeks, in moderately to severely anemic older individuals (≥65 years of age) compared with oral iron alone after major hip surgery. Secondary objective is to evaluate: The safety profile of 3 dose levels of BGE-117 administered orally in older individuals with moderate to severe anemia after major hip surgery.

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 for clarification on how many New Zealand-based participants would take part in the study. The Researcher explained that there would be approximately 10 participants.
2. The Committee asked whether there the study would take place across New Zealand or at one central site. The Researcher said that there would be one site in New Zealand.
3. The Committee asked for clarification on the recruitment process. The Researchers will pre-screen participants through an elective surgery list and approach them if they fit the inclusion criteria of the study. They will be given the participant information sheet (PIS) and will have time to consider before confirming whether they will be a part of the study.
4. The Committee queried how the questionnaires would be conducted, such as either being participant-lead or a member of the research team going through it with them. The Researcher explained that the questionnaires would be conducted by a member of the research team at the follow-up sessions.
5. The Committee asked for clarification on whether there would be prompt follow-up for any issues that may arise (such as deep vein thrombosis or depression scale). The Researcher explained that a research nurse would conduct an assessment and discuss a care plan with the principal investigator (PI).

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 details regarding the wearable activity monitor and any third-party access to data from the monitor to be added to the data management plan (DMP).
2. The Committee requested current evidence of the CI’s indemnity.
3. Please add details on safety protocols during the home visits to ensure the safety of the participant and the research team.

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

1. Please provide further information on the home visits and who will be conducting these.
2. Please include information on the wearable activity monitor.
3. Please include detail on the number of participants in New Zealand.
4. Please consider which contraceptive information is needed for the study, given the study age range. Please consider using the statements in the HDEC [template.](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-reproductive-risks-apr20.docx)
5. Please upload the pregnancy PIS for consideration if this is situation arises, this has not been considered by the HDEC.
6. Please clarify that there will be different dose groups.
7. Please include more information on the use and labelling of the study drug two bottles and how to use them correctly to avoid the risk of participants dosing from one bottle only.

**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 Dr Leonie Walker and Ms Amy Henry.

## General business

1. [add details of each item of general business discussed]
2. The Chair reminded the Committee of the date and time of its next scheduled meeting:

|  |  |
| --- | --- |
| **Meeting date:** | [##MeetingNextMeetingInfoDateTimeOnly##] |
| **Zoom details:** | To be determined |

The following members tendered apologies for this meeting.

* [names of members]

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 [time].