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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 19 October 2021 |
| **Zoom details:** | <https://mohnz.zoom.us/j/86523070649> |

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| **Time** | **Review Reference** | **Project Title** | **Coordinating Investigator** | **Lead Reviewers + Expert reviewers** |
| 11.30 – 11.55am | 2021 FULL 11322 | Mindfulness-Based Cognitive Therapy for family carers of relatives living with dementia- An intervention study | Dr Martin Dvoracek | Catherine/Nicola (Expert) |
| 11.55 – 12.20pm | 2021 TB 11127 | HeartOtago Biobank | Dr Regis Lamberts | Jonathan/Kate/Rochelle (Expert) |
| 12.20 – 12.45pm | 2021 FULL 11110 | ACTION 3 | Dr Tze Liang Goh | Leonie/Sotera/Nicola (Expert) |
| 12.45 – 1.10pm | 2021 FULL 11051 | Dexmedetomidinene verses standard of care (SOC) in the management of agitation in palliative care | Dr Lana Ferguson | Catherine/Jade/Nicola (Expert) |
| **1.10 – 1.30pm** |  | **BREAK (20 MINUTES)** |  |  |
| 1.30 – 1.55pm | 2021 FULL 11184 | Delta-Max | Professor Jamie Sleigh | Jonathan/Rochelle (Expert) |
| 1.55 – 2.20pm | 2021 FULL 11284 | YH003004: A Study to Evaluate YH003 in Combination with Toripalimab in Patients with Unresectable/Metastatic Melanoma and Pancreatic Ductal Adenocarcinoma (PDAC) | Dr Rajiv Kumar | Leonie/Kate |
| 2.20 – 2.45pm | 2021 FULL 11283 | HB0034-01: A Study to Evaluate HB0034 in Health Adult Participants | Dr Christian Schwabe | Catherine/Sotera |
| 2.45 – 3.10pm | 2021 FULL 11329 | M20-178: Myelofibrosis: Phase 3 Study of Navitoclax Plus Ruxolitinib Versus Best Available Therapy (TRANSFORM 2) | Dr James Liang | Jonathan/Jade/Rochelle (Expert) |
| **3.10 – 3.30pm** |  | **BREAK (20 MINUTES)** |  |  |
| 3.30 – 3.55pm | 2021 FULL 11361 | A Study of Midazolam Administered Intranasally Using the NasoSURF Device in Healthy Volunteers | Dr Alexandra Cole | Leonie/Rochelle (Expert) |
| 3.55 – 4.20pm | 2021 FULL 11059 | A Phase 1b Study of ONL1204 Ophthalmic Solution in Patients with Progressing Open Angle Glaucoma | Professor Anthony Wells | Catherine/Kate |
| 4.20 – 4.45pm | 2021 FULL 11120 | Tuning in to Teens in Aotearoa New Zealand | Ms Zara Mansoor | Jonathan/Sotera/Rochelle (Expert) |
| 4.45 – 5.10pm | 2021 EXP 11197 | Mini S Feasibility Study | Dr Andrew Holden | Leonie/Jade/Rochelle (Expert) |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Karen Bartholomew | Non-lay (intervention studies) | 18/07/2016 | 18/07/2019 | Apologies |
| Dr Kate Parker | Non-lay (observational studies) | 11/02/2020 | 11/02/2023 | Present |
| Ms Catherine Garvey | Lay (the law) | 19/03/2019 | 19/03/2022 | Present |
| Dr Sotera Catapang | Non-lay (observational studies) | 11/02/2020 | 11/02/2023 | Present |
| Mr Jonathan Darby | Lay (law/ethical reasoning) | 13/08/2021 | 13/08/2024 | Present |
| Dr Leonie Walker | Lay (ethical/moral reasoning) | 13/08/2021 | 13/08/2024 | Present |
| Ms Jade Scott | Non-lay (intervention studies) | 15/08/2021 | 15/08/2024 | Present |

## Welcome

The Chair opened the meeting at 11am and welcomed Committee members, noting that apologies had been received from Dr Karen Bartholomew.

Also present at the meeting were Ms Rochelle Style and Dr Nicola Swain, Expert Reviewers.

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 21 September 2021 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **2021 FULL 11322** |
|  | Title: | EEG parameters associated with good neurology recovery after elective cardiac surgery in adult patients. |
|  | Principal Investigator: | Dr Martin Dvoracek |
|  | Sponsor: |  |
|  | Clock Start Date: | 26 September 2021 |

Dr Martin Dvoracek 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 aim of this study is to establish a link between electroencephalogram (EEG) recordings and parameters surrounding clinical progress in adults following cardiac surgery. The objectives of the proposed study are:
   1. To explore whether pre-operative EEG parameters indicate poor neurology after cardiac surgery.
   2. To explore whether post-operative EEG parameters indicate risk of poor neurology recovery in patients after cardiac 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 noted that the researcher does not have an academic background in running studies. However, the researcher advised that he has a team supporting him who have an academic background in running studies. There is support from a research fellow and research assistant. The researcher has also completed a six-month EEG course.
2. The Committee asked if any study data will be sent overseas. The researcher confirmed that all study data will stay within the University of Otago.
3. The Committee asked if the peer reviewer, Mr Philip Davis, is independent from the study. The researcher advised that Mr Davis is the cardiothoracic consultant at Southern District Health Board (DHB). The Committee noted that Dr Davis is not very independent from the study but agreed that as the study is a low-risk observational study, it would accept the peer 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. The Committee asked about the recruitment process and how many participants will be under the researcher’s care as they are a clinician. The researcher advised that all participants will be either indirectly or directly under his care because he is a consultant in the Intensive Care Unit (ICU). Participants will be recruited with assistance from the cardiothoracic department. When patients are invited for their elective procedures at least two to three weeks prior to surgery, they will receive the study information. One day prior to the surgery, as part of the routine preparation of showing the patient around the ICU etc., they will go through the study information provided and go through the consent process. After that, they will go through the exclusion and inclusion criteria and start the first neurological exam and other testing. The Committee advised that it is best to have separation between the clinician and researcher roles when obtaining consent. The Committee asked if there was another member of the research team who could consent participants. The researcher confirmed this. There is a non-clinical research assistant who worked on the study documents with the researcher. The researcher also confirmed that he will be easily available if any clinical questions or issues arise during the consent process.
2. The Committee noted that the cultural sections of the application form were not answered well. The researcher incorrectly ticked the box that states the study uses kaupapa Māori methodology (C.3.3); however, it does not. The study also will not reduce racial inequalities solely through participation of Māori or Pacific people (C4). Further, there are more cultural issues beyond just touching the head, which is considered tapu (sacred). The researcher stated that he discussed with a Māori Health Advisor. The Committee stated that researchers are also expected to have knowledge of cultural issues themselves. The Committee suggested that the researcher increase his own knowledge, for example through a cultural course.
3. The Committee noted that the researcher stated in the application form that there is no local sponsor. However, the Committee asked the researcher to confirm that Southern DHB is in support of the research, as someone must take local responsibility.
4. The Committee asked if the researcher is properly insured to run a study i.e., has medical indemnity. The researcher confirmed this. Please upload evidence of medical indemnity.
5. The Committee suggested reviewing the study documents, particularly the Protocol, with the research collaborators.
6. Please re-write the Data Management Plan to match the study. Currently, it refers to the sponsor and overseas investigators; however, this is not applicable to the study.

The Committee requested the following changes to the Participant Information Sheet and Consent Form:

1. Please remove references to the sponsor on page 4.
2. Please remove the paragraph about other additional tests.

**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 2019, 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 2019, 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 Jade Scott.

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| **2** | **Ethics ref:** | **2021 TB 11127** |
|  | Title: | HeartOtago Biobank |
|  | Principal Investigator: | Dr Regis Lamberts |
|  | Sponsor: |  |
|  | Clock Start Date: | 24 September 2021 |

Dr Regis Lamberts 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 Tissue bank application

1. The aim of the HeartOtago Biobank is to promote health-related research relating to the aetiology, diagnosis, treatment and prevention of human cardiovascular disease. The researchers are trying to determine the mechanism of why cardiovascular diseases occur, and specifically in the diabetic and obese heart and hearts with atrial fibrillation, so that in the future these changes can be delayed or prevented from occurring.

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 if any live tissue will be stored in the biobank. The researcher confirmed that no live tissue will go into the biobank. The researcher also confirmed that tissue will only be obtained from live participants, not deceased.
2. The Committee asked what the storage format is for the biobank. The researcher stated that they have one assigned freezer for the tissue. They also have one physical location where they keep all consent forms (locked cabinet, only accessible by the biobank coordinator). Data is stored on the REDCAP database, which only the biobank coordinator has access to. The researcher confirmed that the biobank coordinator will not undertake the clinical procedures of collecting tissue as this is done by the surgeon; however, they will enter the surgical theatre to retrieve and store the tissue once surgically removed.

Summary of outstanding ethical issues

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

1. The Committee noted that there are several relevant guidelines about tissue in the NEAC National Ethical Standards 2019, specifically [Chapter 15](https://neac.health.govt.nz/national-ethical-standards/part-two/15-biobanks/), that are not mentioned in the study documents that the researcher needs to be aware of. Some of these are referenced below. The [Health Information Privacy Code 2020](https://www.privacy.org.nz/privacy-act-2020/codes-of-practice/hipc2020/) is also relevant.
2. The Committee positively noted that there is diverse membership on the Governance Board; however, as both the Governance Board and Executive Committee will be making decisions on access applications, there needs to be diverse membership on the Executive Committee as well (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 15.15 – 15.16*).
3. The Committee acknowledged the researcher’s efforts to include tikanga Māori values and aims. However, this requires more consideration and incorporation. The aims and values currently do not appear to have a deeper connection with tikanga Māori (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 15.16*)
4. The Committee noted that the biobank will involve a large team, with clinicians having access to information as well, and that this may give rise to data/security privacy issues. The Committee discussed with the researcher that there is a difference between the clinical and research contexts. Please be cautious in the documents to not confuse the separate roles of clinicians and researchers. (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 11.23 – 11.24 15.*) Please also amend the documents to accurately reflect the role of participants i.e., that as soon as patients consent to tissue going into the biobank, they will become participants.
5. The Committee enquired about the difference between the archival tissue and prospective collection of tissue. The research started in 2011 and the Committee noted there would be a large amount of archival tissue, and the researcher confirmed this. The researcher also confirmed that they have participant consent (approximately 1000 participants) for the archival tissue. The researcher advised that they are nearly at the 10-year discarding period and there is an opt in/opt out option for participants. Please provide a copy(ies) of the consent form(s) for the archival tissue study.
6. Please note that the 10-year storage period is a minimum, not a maximum period (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 12.13.*).
7. The Committee noted that the researcher had covered several aspects on governance arrangements; however, more detail is required. The Committee advised that for a biobank, governance arrangements should cover (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 15.14*):
   1. the purpose of the biobank and how the biobank will be used
   2. the form (i.e. identifiable, re-identifiable, or non-identifiable) in which the tissue will be stored
   3. the rules of access to the biobank
   4. how researchers or custodians will protect privacy and confidentiality of participants
   5. procedures for returning results, including incidental findings
   6. commercial use and benefit sharing, intellectual property issues and transfer of tissue or material to other institutions or countries
   7. measures to make all aspects of the biobank’s operation transparent
   8. ways in which researchers will be accountable for complying with requirements addressing access, use, and privacy.
8. In terms of governance arrangements, the Committee also suggests referring to the [Stats NZ IDI](https://www.stats.govt.nz/integrated-data/integrated-data-infrastructure/) for guidance.
9. The Committee noted that it is intended that consent will be obtained the day before surgery. This is not a sufficient timeframe given that participants will be asked to donate tissue and some of their data for broad future research. Further, if there might be genetic testing of tissue, all participants and in particular Māori participants may want to discuss this with whānau. Consent should ideally be obtained at least a week before surgery. Please explore whether this is possible. (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 15.8 – 15.12*)
10. Please provide copies of the consent forms that the archival tissue participants signed, as well as the genetic research consent forms. The researcher advised that they do not know what their intentions will be once the 10-year period is reached for the biobank. The Committee advised participants could be re-contacted for re-consenting.
11. The Committee noted that the area of biobanks is complex and evolving rapidly. The Committee suggested that the researcher contact the [Auckland Regional Biobank](https://www.biobank.ac.nz/) as they are currently looking at dynamic consent (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 7.9 – 7.13*).
12. Please include information in the study document about what will be done with any incidental findings. This is particularly important in terms of genetic research (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 15.8 and 15.14*).

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

1. Please re-write the PIS/CF as it is currently written as if this is a study. For example, as this is a biobank, there is no benefit to participants as a result of participation (tissue donation).
2. The PIS/CF needs to reference the correct HDEC.
3. Please remove tick boxes where the statement is not optional. Leave the tick boxes where a statement is actually optional (with a ‘yes / no’ option).
4. Please include data risks to the risks section.
5. Please also be clear about the access to data (clinician access versus researcher access). It is important to be clear about what information will be connected to the biobank.
6. Please clarify rights to access tissue/withdrawal. Please also clarify what happens to tissue/return of results/incidental findings if a participant passes away. (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 14.5, 14.15, and 14.23 – 14.26)*.
7. Please include opt out options as for example, some participants may agree to heart research but not genetic research. (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 14.34)*.

**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 recommended the researcher resubmit to the Northern A HDEC as it has reviewed this initial application and will have more context for the resubmission.

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| **3** | **Ethics ref:** | **2021 FULL 11110** |
|  | Title: | ACTION3 |
|  | Principal Investigator: | Dr Tze Liang Goh |
|  | Sponsor: | Dimerix Bioscience Pty Ltd. |
|  | Clock Start Date: | 24 September 2021 |

Andrew Pilmore 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 of the study is to evaluate the efficacy of a new medication called DMX-200 (repagermanium) in terms of urine polymerase chain reaction and estimated glomerular filtration rate slope in patients with focal segmental glomerulosclerosis (FSGS) who are receiving an angiotensin II receptor blocker (ARB).

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 the researcher had indicated in the application form that the study is not a therapeutic trial. The researcher clarified that was an error as the study is a therapeutic trial.
2. The Committee asked how many participants will be recruited in New Zealand. The researcher stated there will be between five to 10 participants.
3. The Committee noted that the study involves quality of life surveys; however, it was not specified what would be done in the event of patient distress. The Committee asked how the researcher will monitor this in practice. The researcher stated that the companies keep changing the form of data collection. the data tends to be done electronically so the research team does not get to see the participants’ answers, and these remain confidential between the participant and database. However, they do develop strong rapport with the renal community and especially the participants. The researchers see the participants often and get to know them well. The researchers try to ensure that participants are satisfied and if anyone is stressed about issues such as with their kidneys, the research team will intervene.

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 at H1 of the application form, the study is not currently registered. The researcher advised that at the time of filling out the application form it was not registered; however, the sponsor is actioning this. Please provide the registration reference when replying to the Committee’s decision letter.
2. Please provide evidence of insurance under New Zealand jurisdiction.
3. In the Protocol and Participant Information Sheet and Consent Form (PIS/CF) please state the name and location of the central laboratory overseas.
4. The Committee asked if data will be sent overseas. The researcher stated that only de-identified data will be sent overseas. Please specify this in the Protocol and include the location of where the data will be sent.
5. Please provide a separate PIS/CF for Future Unspecified Research. Please refer to the [HDECs template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/future-unspecified-use-tissue-piscf-template.doc) for guidance.
6. Please remove any reference (for example at 7.1 of the Protocol) to the study being discontinued at the sponsor’s wishes. Therapeutic studies where participants are potentially receiving therapeutic benefit must not be terminated simply for reasons of commercial interest (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 11.37*).

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

1. Please clarify the statement on page 10 under ‘Samples for future exploratory research’ about some information about the participant that might be provided (such as date of birth, sex, medical history, and the outcomes of other tests from the study). This is a privacy/confidentiality issue. Accordingly, please specify what type of data/information will be provided (whether the medical history and other test outcomes of the study will bear the name of the participant).
2. Please provide more information about Study Hub. Please ensure that the research team is confident in using the Study Hub service and that its collection, access, and use of data is clearly understood. Please also ensure that participants are informed and can understand it too. There is only brief information in the PIS currently. The Committee suggested reviewing Study Hub’s privacy statements and policies. Some additional wording from those resources may be helpful to include.
3. Please remove the exclusion of the investigational product as a reason not to compensate participants.

**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 PIS/CF, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 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 2019, 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 Dr Sotera Catapang.

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| **4** | **Ethics ref:** | **2021 FULL 11051** |
|  | Title: | Dexmedetomidine verses standard of care (SOC) in the management of agitation in palliative care |
|  | Principal Investigator: | Dr Lana Ferguson |
|  | Sponsor: |  |
|  | Clock Start Date: | 24 September 2021 |

Dr Lana Ferguson and Michael Jameson 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.

A potential conflict of interest was raised by Ms Jade Scott due to having previously worked with Michael Jameson. The Committee was satisfied that there was no conflict and agreed that she could participate in the discussion.

Summary of Study

1. A randomised, unblinded, feasibility study comparing dexmedetomidine with standard of care drug therapy in the management of agitation in a hospice setting. There will be 20 participants, 10 in each arm, and all in the same unit in Waikato. Participation is for 72 hours, at which time best available care will continue.

Summary of outstanding ethical issues

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

1. The Committee noted the researcher’s intention to enrol participants in the study through proxy-consent. It advised that proxy-consent for adults is limited in New Zealand and participants can only be enrolled into research without consent if [Right 7(4) of the Code of Health and Disability Services Consumers’ Rights](https://www.hdc.org.nz/your-rights/about-the-code/code-of-health-and-disability-services-consumers-rights/) is satisfied; whereby any health services provided without the informed consent of the person must be in their best interests. This means that there must be some benefit, or potential benefit, to the participant beyond what they would receive if they were not participating in the research. In addition, if the participant’s views have not been ascertained prior, the researchers will need to take into account the views of those who are interested in the welfare of the participant (i.e., friends and whānau).
   1. Please refer to the relevant law to ensure the enrolment processes meet legal requirements in New Zealand and comply with ethical standards i.e. *Right 7(4) of the of the Code of Health and Disability Services Consumers’ Rights* and *National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 7.59 – 7.75 and paras 6.6 – 6.12*.
   2. Please update the study documentation to detail the revised enrolment/consenting processes which will include the rationale for the best interests argument, process for determining/assessing capacity by someone independent of the study (e.g. clinician providing care), process for gaining views from family/whānau, and process for supported decision-making for those participants who are able to give informed consent with additional support (if the researchers intend to use this model).
   3. Please ensure this structural change is reflected in participant-facing documentation which will include a separate PIS/CFs for the family/whānau providing views of the non-consenting participants.
2. The Committee stated that when the research participant regains capacity to consent, or some capacity to be supported in a decision, as soon as reasonably practicable researchers must give that participant the opportunity to give or decline informed consent to continued participation in the research, and to the use of data or tissue about them that has already been collected *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 7.63).*

**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 2019, 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 2019, para 9.7).*

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

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| **5** | **Ethics ref:** | **2021 FULL 11184** |
|  | Title: | Delta-Max |
|  | Principal Investigator: | Professor Jamie Sleigh |
|  | Sponsor: |  |
|  | Clock Start Date: | 27 September 2021 |

Professor Jamie Sleigh and Jonathan 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. The purpose of this study is to find out if it is feasible to use the slow delta-waves in a patient’s electroencephalogram (EEG) as a guide to helping the anaesthetist decide the best dose of anaesthesia during an operation. 220 participants for the New Zealand pilot study will take part at Waikato Hospital.

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 researcher’s clarification that the application for review by HDEC includes both the pilot study and the subsequent full 200 participant study.
2. The Committee advised that an exclusion criterion mentioned in the MRC documentation appeared to be missing from the protocol, i.e., people with a history of VTE and who are using hormone replacement therapy or oestrogen-containing oral contraceptives. The researcher clarified that the possibility of these participants being at higher risk of DVT developing is no longer valid which is why it is not included in the protocol.
3. The Committee queried what the resource implications are for the hospital if two anaesthetists are required for one surgery. The researcher clarified that only one anaesthetist is required as per the standard procedure.
4. The Committee noted that the formal consenting process will be completed on the morning of participant’s surgery and queried how participants will be given sufficient time to discuss and consider their involvement.The researcher clarified their enrolment process and that participants will be given the study information well in advance and will be given the opportunity to ask questions prior to their surgery date.
5. The Committee noted the researcher’s confirmation that the model will be optimised, and iterative changes made, between the pilot study and the full study.
6. The Committee asked for clarification on validation of the model in New Zealand when it was trained on a United Kingdom population. The researcher explained that the model itself is simple, using a standard drug response model that is not predictive. He added that it is collecting data on the delta-waves being produced on a standard EEG monitor and displaying it in a quantitative, and more readable, format.

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 what happens if an anaesthetist is confident with drug a dose range but the predicted delta-max from the model says it should be in a different range. The researcher confirmed that the anaesthetist/clinician can override the model and administer the dosage based on their expertise. Please clarify this is in the protocol and how the model’s prediction failure will be recorded.
2. The Committee advised the protocol should be a standalone document that includes all relevant information for this study rather than cross-referencing protocols of previous studies. Further, much more detail from the MRC documentation needs to be incorporated into the protocol as it is missing significant detail for the New Zealand part of the study and there are inconsistencies across the documents *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 9.7).*
3. The Committee advised there is no detail in the protocol about the pre-existing audit health data referenced throughout the study documentation. For example, where it is coming from, what it comprises of (e.g. identifiable vs de-identified information), how it will be used and if consent has been gained for secondary use of this data. The researcher explained that the secondary use will involve standard de-identified data routinely collected at the hospital (e.g. pain point and nausea rate of hysterectomy patients) and comparing this dataset against the study dataset. The Committee requested the protocol details this re-use of (audit) data and to ensure it complies with *National Ethical Standards for Health and Disability Research and Quality Improvement 2019, Chapters 12 and 13).*
4. The Committee advised there was no detail in the study documentation on how the researchers will initialise the model parameters in a participant-specific manner. The researcher explained that there is always variations and fluctuations between individuals, and this will be the main problem impacting feasibility. The researcher further explained that an individual baseline will be established and recorded on the EEG while the participant is awake.
5. The Committee advised that there are inconsistencies in the study documentation on the stopping rules that may impact whether or not the study has been successful and that require clarifying in the protocol:
   1. The documentation says any unexplained awareness on the Brice questionnaire in either phase will result in re-evaluation of the study. It also states any unexplained awareness on the Brice questionnaire will result in early termination of the feasibility study.
   2. Any unexplained intraoperative awareness will result in early termination and/or re-evaluation of the study but, on the other hand, the documentation says a positive IFT rate of more than 5% is unacceptable if the SWAS-BPM is able to prevent awareness.
   3. The protocol states, “The presence of ANY positive responses for the volitional isolated forearm test or Brice interview will be enough to disprove the basic premise of delta-max as an indicator of the brain’s inability to form conscious awareness” and,” In the unlikely event there was a positive response in the IFT or Brice questionnaire – and the patient was clearly in SWAS – the study would be terminated as this would prove SWAS did not mean loss of sensory conductivity.
   4. In other documentation it says if the forearm test shows a participant is not unconscious despite reaching predicted delt-max “This will result in an immediate formal review, and the study will be terminated unless there are extenuating circumstances.” However, these extenuating circumstances are not described.
   5. The protocol also states, “A successful study outcome is defined as an incidence rate of zero positive IFT responses for patients that have achieved delta-max/SWAS.” However, a primary endpoint, “To confirm that it is feasible to achieve delta-max in a timely manner in 220 routine surgical patients undergoing general anaesthesia”.
6. The Committee noted the definition of adverse events in Appendix 3 of the protocol seems to be a general definition rather than study specific. Please amend.
7. The Committee noted the data and tissue management plan (DTMP) does not accurately capture the data and tissue management requirements of this study (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 12.15a and 14.17.)* The Committee requested the following changes to the DTMP:
   1. Please delete template instructions to researchers.
   2. Please detail what type of data will the MRC Panel will receive who appear to be acting as an independent data management committee.
   3. Please clarify where the Delta-wave Standard Operating Procedure manual is on page 4.
   4. Please clarify on page 5 where the EEG data will be kept indefinitely which will form the basis for an international collaborative database to facilitate future EEG research.
   5. Please detail what third parties will be working with, or for, the sponsor, including the sponsor’s subsidiaries and affiliates and third-party researchers on page 7.
   6. Please amend section 7.3 on page 8 as there is no section 8.5 and the reference to section 8.2 is incorrect.
   7. Please redraft section 7.5 on page 9 to ensure it is study specific as it appears to be a copy and paste response (e.g. for example, this is not relevant “unspecified purposes which are related to the condition under study”.
   8. Please clarify how the EEGs will be de-identified and transmitted to the UK (e.g. through REDCap).
   9. Please include information about the open-source EEG and anaesthesia database (ACCESS).
   10. Please provide more information about the model and how privacy and security will be addressed.
8. The Committee advised that as anaesthetists are participating in the study, they will require a separate participant information sheet and consent form (PIS/CF) detailing their involvement and what is required of them.
9. The Committee advised that Māori cultural aspects of the study have not be adequately detailed such as Māori data sovereignty. Please ensue formal Māori consultation occurs prior to the study starting to ensure it is appropriate for a New Zealand context *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 3.7).*

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF) in addition to those mentioned above *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 7.15 – 7.17)*:

1. Please more clearly explain what will happen during the procedure that is specific to the study (e.g. study doctor will be sitting to the side with a laptop, giving advice to anaesthetists based on delta-wave readings, etc.). Please also reassure participants that this advice will be taken at the anaesthetist’s discretion.
2. Please provide more information on what the study involves (the procedures) on page 3. That is, the isolated forearm test/ the wiggle fingers test and how often it will be done, the times at which the Brice questionnaire will be done, that some bloods will be kept at Waikato for propofol analysis, etc.
3. Please more accurately describe the purpose of the study, which is not only feasibility, but also to determine whether looking at the delta-waves allows the model to achieve the optimal dose per person of the anaesthetic drugs and to essentially provide data to improve the model.
4. Please include information about the development of the model.
5. Please detail how the consenting process will work on the day of surgery.
6. Please address issues relevant for Māori, such as the potential risks and cultural issues associated with sending and storing data and tissue overseas, and that there may be no New Zealand representation on overseas governance committees.
7. As this is the pilot part of phase 2 with 20 participants, it is not accurate to state on page 1 “The study will prove if it is feasible to look at these waveform patterns to guide the anaesthetic you are receiving, by fine tuning the amount of anaesthetic amounts during surgery”. Please amend.
8. Please replace references to ‘patients’ with ‘participants’. Please also use the pronoun ‘you’ and second-person perspective where appropriate to personalise the document.
9. Please detail all the risks more clearly including intraoperative hypotension from excess anaesthesia, increases in total anaesthetic time, and explaining if you may be holding participants at delta wave for a period of time and what the implications.
10. Please move accurately describe the inclusion criteria as per the protocol and other documentation.
11. Please clarify the placement of the EEG stickers (i.e. will they be EEG stickers on the forehead or will they be on the scalp).
12. Please use lay terms to describe the benefits as most people will not understand ‘smoother intraoperative course’ on page 4.
13. Please use the standard wording for ACC compensation in the [HDEC’s PIS/CF template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc).
14. Please review the 'What happens to my information section' of [HDEC’s PIS/CF template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc) and incorporate relevant components into the PIS/CF. This section should align to the information in your data management plan. Please ensure issues such as the risk of data / confidentiality breach, access to identifiable and de-identified data, data-linking, withdrawal of data, rights to access and correct data, IP rights, and future uses of data are addressed.
15. Given anonymised data may go to open-access registries, it is not correct to state: “Any information we collect with this study that can identify a patient will remain confidential and we will only use this information for the purpose of this study” on page 4. Please amend.
16. On page 4, it is not clear from the following statement whether the health records are for the particular participant or for other people, “For this study we will want to look at patient health records stored by the hospital.” Please be more specific about what information from which records will be collected and for whom.
17. Please include participants right to receive a summary of results if they choose.
18. Please include information on what incidental findings might arise.
19. Please ensure all consent items have previously been explained in the body of the information sheet. The consent form should not include any new information.

**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 recommended the researcher resubmit to the Northern A HDEC as it has reviewed this initial application and will have more context for the resubmission.

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| **6** | **Ethics ref:** | **2021 FULL 11284** |
|  | Title: | YH003004: A Study to Evaluate YH003 in Combination with Toripalimab in Patients with Unresectable/Metastatic Melanoma and Pancreatic Ductal Adenocarcinoma (PDAC) |
|  | Principal Investigator: | Dr Rajiv Kumar |
|  | Sponsor: | Eucure (Beijing) Biophama Co., Ltd. |
|  | Clock Start Date: | 28 September 2021 |

Dr Rajiv Kumar and Courtney Rowse 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. A phase 2, multi-centre, open-label study to evaluate the safety and efficacy of YH003 in combination with Toripalimab (anti-PD-1 mAb) in patients with unresectable/metastatic melanoma and pancreatic ductal adenocarcinoma (PDAC).

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 researcher’s confirmation that they will collect local ethnicity data for the New Zealand arm of the study.

Summary of outstanding ethical issues

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

1. The Committee noted the protocol references accessing archival tissue, but this is not mentioned in the Participant information sheet and consent form (PIS/CF). The researcher will clarify this with the sponsor and add to the PIS/CF if required.

The Committee requested the following changes to the PIS/CF in addition to those mentioned above:

1. Please state up front in the PIS/CF that YH003 has only been tested in 16 people (in the world) to date.
2. The alternatives to participation are quite detailed and may not be available to all participants. Please consider stating that there are other approved treatment options available and that they can discuss these with their study doctor.
3. Please categorise the risks of YH003 (e.g., mild / moderate / severe) to make it easier to read for participants.
4. Please add the locations of where the data will be sent.
5. Please clarify the statements inferring the drug is already approved as the specific drug is not approved in New Zealand.
6. Please clarify when the participant will need to visit the unit for the PK sampling on page 6 (i.e., day one and two).
7. If relying on Medicines New Zealand’s guidelines, the sponsor must be a member of Medicines New Zealand and have agreed to abide by these guidelines. Please clarify with the sponsor and amend the compensation statement in the PIS/CF if required.
8. Please state that participants may be tested for COVID-19 if this is a possibility.

**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 PIS/CF, taking into account the feedback provided by the Committee *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 7.15 – 7.17).*

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| **7** | **Ethics ref:** | **2021 FULL 11283** |
|  | Title: | HB0034-01: A Study to Evaluate HB0034 in Health Adult Participants |
|  | Principal Investigator: | Dr Christian Schwabe |
|  | Sponsor: | Shanghai Huaoto Biopharmaceutical Co., Ltd. |
|  | Clock Start Date: | 29 September 2021 |

Dr Christian Schwabe and Courtney Rowse 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. HB0034 is being developed for the potential treatment of autoimmune inflammatory diseases including generalised pustular psoriasis (severe form of skin disorder characterised by fluid filled bumps), inflammatory bowel disease (conditions involving inflammation of the intestine), systemic lupus erythematosus (autoimmune disease involving multiple organs), and fibrosis (chronic inflammatory reaction resulting in thickening or scarring of the tissue). Inflammatory conditions such as these are thought to result from an abnormal immune reaction, whereby the release of inflammatory cells is upregulated.
2. HB0034 is a drug in the class known as ‘Monoclonal Antibodies’ which are special proteins that reassemble a part of the body’s natural immune system. HB0034 is being developed to treat these inflammatory conditions by inhibiting the release of specific inflammatory cells to decrease the level of inflammation.
3. The study objectives are to:
4. evaluate how safe and well tolerated HB0034 is, following a single dose in healthy participants
5. measure levels of HB0034 in the blood over time (pharmacokinetics), following a single dose in healthy participants
6. assess the body's immune response (immunogenicity) to HB0034, following a single dose in healthy participants.

Summary of resolved ethical issues

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

1. The Committee asked about the recruitment and inclusion criteria regarding the mix of ethnicities, and if there will be targeted recruitment based off ethnicity. The researchers explained they are not excluding anyone on the basis of ethnicity.
2. The Committee asked about the flexibility of timing of payments to participants so that they are not undertaking five-night stays without reimbursement until after study completion. The researchers stated that they will add some wording to better explain the payments and provide more flexibility to the frequency of the payments for participants, including participants who experience hardship.
3. The Committee enquired about the situation regarding vaccination against COVID-19 for potential and current participants. The researchers explained that for this study the participants are allowed to be vaccinated prior to entry and can also plan to have the vaccine if they have not received it while they are participating in the study. However, participants cannot receive the vaccine two weeks prior to dosing and within four weeks following the dosing.
4. The Committee asked about the vital signs around the fifth day and if they will be taken from participants which may serve as the baseline result to be compared with the succeeding results during follow-ups (related to efficacy end point). The researchers explained that there will be no vital signs taken on the fifth day as per protocol and per the ISF. The vitals on the fifth day are not considered necessary for safety.

Summary of outstanding ethical issues

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

The Committee requested the following changes to the Protocol:

1. Please specify the amount of blood taken for PK per time point.
2. Please include fasting on the designated time/schedule (under study restriction) before participants can be admitted into the clinical ward to be consistent with the Participant Information Sheet and Consent Form (PIS/CF).
3. Please refrain from using ‘subject’ or ‘patient’ when referring to the study participant(s) to avoid confusion and for consistency. Participant(s) is the correct term once consent has been obtained to participate in the study.

The Committee requested the following changes to the Data and Tissue Management Plan:

1. At section 7.8.3, please clarify the reference to data being sent to Australia, Canada, India, Singapore, and the United States (in addition to China) as this is not referred to elsewhere.

The Committee requested the following changes to the PIS/CF:

1. Please indicate the amount of blood/withdrawal for the positive ADA participant/s and the total amount for this procedure.
2. On page 7, please change ‘aggressing’ to agreeing.
3. On page 8, please amend the wording of 3.1 to reflect healthy volunteers, not patient participants. Currently, this section states ‘your condition may get better, but it could stay the same or even get worse’.
4. Please include in patient information sheet participant’s GP to be informed of his/her enrolment to the study.

**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 PIS/CF, taking into account the feedback provided by the Committee *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 7.15 – 7.17)*
* please update the study protocol, taking into account the feedback provided by the Committee (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 9.7*).

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| **8** | **Ethics ref:** | **2021 FULL 11329** |
|  | Title: | M20-178: Myelofibrosis: Phase 3 Study of Navitoclax Plus Ruxolitinib Versus Best Available Therapy (TRANSFORM 2) |
|  | Principal Investigator: | Dr James Liang |
|  | Sponsor: | AbbVie Limited |
|  | Clock Start Date: | 29 September 2021 |

Dr James Liang and Shilpa Jain 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 purpose of this study is to evaluate how well the investigational product (Navitoclax) works in combination with Ruxolitinib when compared to best available therapy on participants with Myelofibrosis. The study consists of two arms.
2. 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 if the study drug (Navitoclax) is already used in New Zealand as best available therapy. The researcher advised that it is not. Navitoclax is a new drug that they are trialling with Ruxolitinib. Ruxolitinib is currently available in New Zealand. The Committee asked what the risks/benefits are for participants who are already taking Ruxolitinib and are randomised in the study (Arm B). The researcher stated that participants in Arm B probably will not receive any benefit from the study as they will receive treatment they are already being provided with (Ruxolitinib).
2. The Committee asked how many participants are expected to be in New Zealand. The researcher stated that given Myelofibrosis is a rare disease, they expect there will be approximately four to six participants. The Committee was satisfied with the insurance amount available for this number of 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 noted that several issues with the documents that were identified by the Northern B HDEC in relation to the earlier TRANSFORM 1 study have not been taken into account for this study’s documents. The Committee recommends that all requests from the Northern B HDEC, as relevant to this study, be addressed.
2. The Committee asked if the researcher agreed with the sponsor’s re-evaluation of the benefit and risk valuation for the study in regards to COVID-19 in that participants receiving Navitoclax may be at an increased risk for COVID-19 infection or experience serious illness if infected. The researcher stated that overall, the benefits outweigh the potential side effects from combining treatment together. Please explain this in the Participant Information Sheet and Consent Form (PIS/CF) (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 7.15*).
3. The Committee referred to the advertisement letter to patients from the researcher who is also the clinician. This should be avoided if possible and someone else from the research team (in a non-clinical role) should send it. This is to manage the researcher/clinician conflation and prevent the patient from feeling obliged to participate. (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 11.23 – 11.24.*) The letter should also mention that the study is sponsored, mention Medsafe, and that a PIS/CF is available.
4. The Committee noted that there are inconsistencies in the study documents about which biomarker analyses are mandatory and which are optional (as noted by the Northern B HDEC for the TRANSFORM 1 study). The Protocol clearly states that some of the biomarkers are optional. There is only one paragraph in the main PIS/CF about biomarkers. This is insufficient and requires more detail. There is also no explanation of what cytogenetic testing is – please also explain in lay language what translational research is (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 14.27 – 14.34, 14.37 – 14.41.*) There is more detail about biomarker research in the Optional Research PIS/CF, but this information is insufficient too. Further, the ability to withdraw consent from the use of tissue (mandatory or optional) is confusing. Please make this very clear in the documents.
5. The Committee noted that the researcher did not include a plan for the possibility that participants may experience distress, depression, anxiety, or suicidal ideation (as might be revealed when completing the questionnaires). This possibility was recognised in the application form; however, more detail/a formalised plan is required in the actual study documents about how this will be managed. Please include this in the Protocol or in a separate document (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 8.8 – 8.9.*)
6. The Committee noted that none of the documents, including the Data and Tissue Management Plan (DTMP), state where tissue will be stored post-analysis. Please rectify this as it is a significant omission (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 7.57 – 7.58*).
7. The Committee referred to the DTMP and noted the following issues (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 14.16 – 14.18*):
   1. There is nothing about the Rave data capture system. This is a significant omission that must be rectified. The Protocol does mention Rave but provides no material details. For the DTMP, please include more information about Rave, for example whether the information will be identifiable (it should not be since the sponsor will have access to it).
   2. Section 7 – please clarify what identifiers will be used for the screening and safety tissue samples (and their results).
   3. Section 10 – it is not clear where tissue will be stored post-analysis and that the samples will be retained until testing is complete or no longer than 20 years. Please clarify this.
   4. Section 12 – this is incorrect as there will be data and tissue for future unspecified research in the optional study. Please amend.
8. For the ‘survival follow-up pathway’, please provide clearer information about the types of public databases that will be searched. For this pathway, please also take into account the Northern B HDEC’s feedback about contacting family members.
9. Please remove any reference to the study being discontinued at the sponsor’s wishes. Therapeutic studies where participants are potentially receiving therapeutic benefit must not be terminated simply for reasons of commercial interest (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 11.37*).
10. Please note that under New Zealand law, you cannot have a legally authorised representative consent to research on behalf of someone else. Please remove any reference to this in the study documents.
11. Please only submit pregnancy PIS/CFs to HDECs for review only if a participant becomes pregnant. If this happens, please submit an amendment through the post-approval pathway.

The Committee requested the following changes to the PIS/CF *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 7.15 – 7.17)*:

1. The DTMP states that clinically significant findings may result from the tests and assessments required as part of the study. Participants will be informed of any unexpected results/findings by the investigator. The investigator will take appropriate action and provide follow-up when required. However, nothing is said about this in the PIS/CFs – please rectify. *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 14.15, 14.23 – 14.26, 14.37 – 14.41).*
2. Please include more overseas warning statements as per the [NEAC Standards](https://neac.health.govt.nz/national-ethical-standards/part-two/12-health-data/) (paras 12.14 to 12.16) that set out what participants must be informed of in terms of overseas data protection etc.
3. Please inform participants that as part of the screening/routine clinical practice, results of HIV and hepatitis are notifiable the Medical Officer of Health as per the Health Act 1956.

Main PIS/CF

1. Please clarify what form the study treatment will be provided in i.e., tablet form plus the dose amount(s).
2. Please provide more information about what happens at a ‘treatment completion visit’, at a ‘safety follow-up visit’, unspecified post-treatment tests for participants stopping the study drug, and at 24 weeks.
3. For the listed side effects, please include the frequency at which those side effects are encountered and their severity.
4. Please note that the contraception wording in the PIS is not the same as that used in the [HDECs template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc).
5. There is insufficient information about whether return of tissue or karakia is possible *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 7.18 and 14.17).*
6. On page 3, it states that in some countries other locally available formulations may be available. The researcher clarified that this is not applicable in New Zealand as the only formulation there is access to is Ruxolitinib. Please clarify and amend this statement to reflect the New Zealand setting, including making clear that participants who are randomised to Arm B will remain on their current therapy.
7. On pages 7 to 9, the tables provided appear to be copied directly from the Protocol. These contain several abbreviations and acronyms. Please amend the tables so that they are written in plain lay language.
8. On page 22, there is confusion about the use of the term ‘generic code’ in relation to participants’ data that is shared with the sponsor. Please state ‘unique code’ instead. This is also what is explained in the DTMP.
9. On page 23, the use of the term ‘personal data’ for this section is confusing as personal data will not be shared with the sponsor. Please remove the word ‘personal’ and clarify this. Also, the concept of a ‘controller’ is a European concept that is not used in New Zealand. There are also some additional powers and rights mentioned in the PIS/CF that are not available in New Zealand. Please amend to reflect the New Zealand setting and refer to the HDECs template for guidance.
10. On page 25, please correct the statement to say that participants do have the right of access and correction to their personal information under the Privacy Act 2020. Currently, the statement implies that that they only ‘may’ have that right.
11. On page 25 and 28, some of the rights referred to are not available under New Zealand law.
12. On page 27, under the heading ‘Who is funding the study’ it is not correct to state that the sponsor/companies will be provided with biological samples or data generated from analysis of the samples. It is only coded samples and data.
13. On pages 27 to 28, the last two paragraphs under the heading ‘Personal Data’ are contradictory. Either the data prior to withdrawal will be used as pat of the research results or may be required to do so. The implication from the two paragraphs is that there is a legal requirement to do this. The DTMP states that data will continue to be used post withdrawal.

Optional Research PIS/CF

1. Please be consistent about the scope of what is being proposed for the optional research i.e., whether this is only in relation to Myelofibrosis/the study drug or whether it is broader/completely open.
2. Please be clear as to whether participants will be provided with results from the Optional Research study. Some documents state they will be provided with results, but others do not.
3. On page 3, it states that, ‘The biological samples (such as blood, urine, stool, and tissue) that we collect from you for the purpose of this research will be stored, processed and used as described in this document’. However, for the study the Protocol states that only blood will be used for the optional research. Please clarify this and remove the additional types of samples. Please also review the full document to ensure that there is only reference to blood samples, not biological samples (for example in the ‘What if I withdraw?’ section).
4. On page 3, please state that the study doctor will inform the participant’s general practitioner (GP). Please remove the statement, ‘we strongly recommend that you inform your doctor’. Also, please replace any reference to the participant’s ‘local doctor’ with ‘GP’ *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 7.18)*.
5. Please clarify whether any clinical data will accompany the samples. This appears to be the case based on the CF but please explain in the body of the PIS.
6. Please clearly describe the type of genetic testing.
7. On page 5, there needs to be a data section tailored specifically to this Optional Research study. The information provided is currently insufficient. Please do not just refer to the main PIS/CF for this information (this was also done on page 6). All information needs to be in each PIS/CF.
8. On page 3, for how the samples will be destroyed, please state that samples will be destroyed by incineration (as stated in the DTMP).
9. On page 4, there is more reference to ‘personal data’. Please amend this as per the Committee’s comments for the main PIS/CF.
10. On page 6, it states that participants will not be given their results; however, this contradicts what is stated elsewhere.
11. On page 7, please amend the reference to rights which are GDPR based – these must be tailored to the New Zealand setting.
12. On page 9, it requests consent to biological (change to ‘blood’) samples being stored ‘indefinitely’. Please amend as the DTMP and Protocol state that samples will be retained until testing is complete or no longer than 20 years.
13. On the CF, the statement where participants volunteer to provide their blood samples implies that this is optional. However, there can be no participation in this study is the participant does not agree to provide their samples.
14. Please review the document for spelling mistakes and grammatical errors.

**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 recommended the researcher resubmit to the Northern A HDEC as it has reviewed this initial application and will have more context for the resubmission.

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| **9** | **Ethics ref:** | **2021 FULL 11361** |
|  | Title: | A Study of Midazolam Administered Intranasally Using the NasoSURF Device in Healthy Volunteers |
|  | Principal Investigator: | Dr Alexandra Cole |
|  | Sponsor: | AFT Pharmaceuticals Ltd. |
|  | Clock Start Date: | 30 September 2021 |

Dr Alexandra Cole, Dr Chris Wynne, Sharmin Bala, and Courtney Rowse 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 test an experimental intranasal (in the nose) drug delivery device, named NasoSURF, that is being used to deliver the drug, Midazolam (MDZ). MDZ is being used for the treatment of anxiety and stress related to surgical or diagnostic procedures, through its sedating (calming) action.
2. The purpose of this study is to:
3. evaluate how safe and well tolerated MDZ administered intranasally using the NasoSURF device is, compared to IV administration, in healthy volunteers
4. measure levels of Midazolam in the blood over time, following a single dose intranasally using the NasoSURF device / Midazolam IV
5. measure the body’s response to a single dose of MDZ administered intranasally using the NasoSURF device / Midazolam IV
6. assess the amount of sedation caused by MDZ administered intranasally using the NasoSURF device / Midazolam IV.

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 there is a chance of bias because the Observers Assessment of Alertness/Sedation (OAA/S) assessments are not blinded. The researcher stated that the objective of this study is to look at the PK data, so potential bias will not affect the data for the study objective.

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 if the specific iteration of the device has been trialled before. The researcher advised that it has in some animal studies. The Committee noted that the novelty factor is Midazolam being delivered through the device. Please mention the animal trials in the Participant Information Sheet and Consent Form (PIS/CF).
2. The Committee asked if the research team will arrange transport for participants after Midazolam dosing. The researcher confirmed this. They will dose the participants first thing in the morning and keep them in the unit for about 12 hours. It is expected that the effects would wear off by this point; however, standard advice post Midazolam is to not drive or operate machinery for at least 24 hours. The research team will ensure that participants take up the offer for provision of taxis/Ubers to bring them to and from the unit. Please ensure that this information is included in the PIS/CF. Further, the researcher advised that the research team are fully equipped in the case of an emergency. They have the antidote available on the ward, and as part of the protocol, medical and nursing staff will regularly undertake assessments about sedation.
3. The Committee referred to the advertisements and asked that the 13-hour clinic visits be stated more explicitly. Please also state that the study involves a nasal device for administration of Midazolam.
4. The Committee asked whether the device is class I or II because the documents are inconsistent. The documents state that the device is registered with the FDA as class I but also state that the sponsor is seeking class II registration. Please check this with the sponsor.
5. The Committee asked if the aerosol droplets can escape i.e., onto other patients in the unit. The researcher advised that they have emailed the sponsor about this question. Please provide this information to the Committee. The researcher also noted that if COVID-19 cases are in the South Island, participants will not be admitted into the ward unless they have a negative COVID-19 PCR test.
6. The Committee referred to the Data and Tissue Management Plan (DTMP):
   1. On page 3, Canterbury Health Laboratory is not a CI. Please list this in the laboratory section.
   2. In reference to Section 7.1 on page 10, please do not use more identifiers than necessary on the samples. There are currently too many. *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 14.19)*. In relation to this, page 10 of the PIS/CF needs to be amended as well.
   3. Sections 9.1 and 9.2 are inconsistent with other documents. For example, on page 12 of the PIS/CF, it states that ‘The following groups may have access to your coded information, which will be sent and stored outside NZCR premises: De-identified information in electronic form will remain on a secure platform and will be retained indefinitely/. Please amend for consistency.
   4. Section 12.2.1 does not make sense as there is no future unspecified research.
7. Please provide an update on Māori consultation, which had not occurred at the date of study submission, similarly with Pasifika engagement.
8. Please remove any reference to the study being discontinued at the sponsor’s wishes. Therapeutic studies where participants are potentially receiving therapeutic benefit must not be terminated simply for reasons of commercial interest (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 11.37*).

The Committee requested the following changes to the PIS/CF:

1. On page 2, please consider amending the wording ‘for those who are not comfortable being pricked’. The Committee suggested changing the wording to ‘not comfortable with needles’.
2. Under the heading ‘What would your participation involve?’, please include information about the length of visits before the table.
3. Please clarify how far apart the visits are. The washout period between dosing is 48 hours; however, this is not clearly stated. It is also unclear when the second visit will occur in relation to the first.
4. Please include the frequency of side effects and their severity.
5. Please consider rewording the COVID-19 vaccination advice (‘you may receive the vaccination at the discretion of the investigator’).
6. Please mention the intravenous cannula.
7. Please do not raise any new issues in the CF if they are not already addressed in the PIS. For example, please include in the body of the PIS, that the research team will inform the participants’ general practitioner if any significant abnormal results are found during the study.
8. Please include in the CF that results of the study will be provided to participants if they wish.
9. Please inform participants that as part of the screening/routine clinical practice, results of HIV and hepatitis are notifiable the Medical Officer of Health as per the Health Act 1956.
10. Please amend the compensation section and remove reference to the Medicines New Zealand Guidelines as this study is a device trial.
11. Please note that the contraception wording in the PIS is not the same as that used in the [HDECs template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc).
12. Please review the document and ensure that it is written in lay language.
13. Please fix any spelling mistakes and grammatical errors (for example on page 4 of the table, it states ‘stud drug’ not ‘study drug’).

**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 PIS/CF, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 7.15 – 7.17).*

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

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| **10** | **Ethics ref:** | **2021 FULL 11059** |
|  | Title: | A Phase 1b Study of ONL1204 Ophthalmic Solution in Patients with Progressing Open Angle Glaucoma |
|  | Principal Investigator: | Professor Anthony Wells |
|  | Sponsor: | ONL Therapeutics, Inc. |
|  | Clock Start Date: | 01 October 2021 |

No members from the research team 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 purpose of this study is to demonstrate safety and tolerability of ONL1204 Ophthalmic Solution in patients with progressing open angle glaucoma. The study also aims to assess the efficacy and the pharmacokinetics of ONL1204 Ophthalmic Solution in male and female participants aged 18 years and older.

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 what is meant by the following statement: “if any additional analyses are requested, you will have the right to refuse to these additional tests being carried out”. Do the researchers envisage requesting more tests on already collected samples?
2. The Data Tissue Management Plan (DTMP) needs to be NZ-specific, e.g. section 3 should refer to relevant NZ Organisational Data Governance Oversight (not just let this fall under "any other local applicable regulations").
3. The DTMP needs to say how long tissue will be stored for.
4. Specify the central laboratory where tissue samples to be analyzed.
5. Why can the sponsor receive participant identifiers (date of birth)? The Sponsor should not receive information that identifies participants.
6. The Committee noted that the rationale and methodology for testing the new imaging technique and ANX776 is not well described, particularly in the PIS, and why they are doing two studies at the same time.
7. The Committee noted that there is no reimbursement for some very long clinic visits and that this is unfair.
8. The Committee was concerned about the use of “Patient Go” and considered that this was not well described in the application. In particular:
   1. For patients who do not use it, do they receive credit to their bank accounts?
   2. How will their privacy and confidentiality be ensured, noting that they are providing sensitive information to Illingworth Research Group?
   3. Why do participants have to pay a fee if they want to get their money as cash from an ATM?
   4. The agreement to sign is excessive and onerous on the participant, and may result in the participant choosing not to read the agreement before signing. Participants are subject to non-straightforward ‘rules’ around collection and use of identifiable data, and complicated claiming procedures. If sites are intending to use the services, the onus is on them to clearly understand and explain these, and to be confident that the material provided is suitable for a NZ setting and understandable to participants.
   5. There is a concerning lack of assurance as to security of data, e.g. “any message or information you send using the App may be read or intercepted by others….”.
   6. Why do participants only have 30 days to make a claim?
   7. Data is going overseas and will be stored for seven years, yet there is no mention of this in the PIS.
   8. Data can be used for business purposes without consent.
   9. Why does Patient Go need access to photos and videos?
9. Receipts for reimbursement should not be required, and please also consider meals etc. for the days when participants cannot leave the site for the whole day, rather than requiring receipts or their agreement to use the Patient GO card.
10. Confirm SCOTT approval has been sought for both experimental aspects of the study, the IMP and the DARC imaging.
11. Confirm that remote access by the CRO (especially during Covid) is appropriately controlled, e.g. that they have no ability to download or copy documents; that there is monitoring of access by the site.
12. Is there standard of care for the non-study eye? If there is will it not interact with the intervention of the study eye?
13. Please update the study protocol and DTMP to clarify the information queried above (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 9.7, 12.15*).

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF) (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 7.15 – 7.17)*:

1. Add the early phase statement, as per the HDEC PISCF template.
2. Tell participants there are 3 groups: 2 different dose groups and one 'sham'.
3. Explain the acronym DARC and what it is the first time the experimental imaging is referred to on p2.
4. Clarify how the imaging is being ‘tested’ in the study, where they images are sent to, and where the central reading centre is located.
5. Make notification to GP mandatory.
6. Discussion of Patient GO needs further consideration and if used, rewording ("our Privacy policy"). As above, responsibility rests with the researchers. The Privacy Policy that participants are referred to is European-focussed and excessively long.
7. Please clarify what information is being collected, who will have access to it, and how long it is going to be stored.
8. On page 9, please refer to the number of participants in prior studies who have been administered ONL1204 in the pertinent doses.
9. On page 2, please inform how many people have had ANX776 solution used so far.
10. Use the standard contraception wording from the HDEC PISCF template.
11. Include the addresses of overseas labs.
12. Page 12 refers to a form for withdrawing, though later acknowledges orally withdrawing. Confirm that participants are not required to withdraw in writing.
13. Remove the reference to ending the study for commercial reasons. Studies cannot be ended for commercial or administrative purposes in NZ.
14. If ONL Therapeutics is not a member of Medicines NZ the compensation section will need to be reworded.
15. Include the total amount of blood taken per participant across the whole study.
16. Explain to participant the selection of study eye if both eyes are affected by the condition (only one eye to be enrolled).
17. Explain to participants the standard of care (if present) in the non-study eye.
18. Please describe the risks of being on no treatment for glaucoma for 39 weeks.

**Decision**

This application was *declined* by consensus, as the Committee did not consider that the study would meet the ethical standards referenced above.

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| **11** | **Ethics ref:** | **2021 FULL 11120** |
|  | Title: | Tuning in to Teens Aotearoa New Zealand |
|  | Principal Investigator: | Ms Zara Mansoor |
|  | Sponsor: |  |
|  | Clock Start Date: | 05 October 2021 |

Zara Mansoor and Elliot Bell 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 main aim of the study is to evaluate the impact of Tuning in to Teens (TINT) as an addition to care for young adolescents presenting to Child Adolescent Mental Health Services (CAMHS) in Aotearoa New Zealand (NZ).
2. The objectives are:

1. To determine meaningful outcomes from a service-user perspective when evaluating the programme (Co-design of outcome measures).

2. To compare TINT (as an enhancement to usual care) to usual care alone for young adolescents in CAMHS (Pilot randomised control trial)

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 concern about the small sample size for the study, especially if any participants withdraw. The researcher responded that this was the minimum possible sample size due to scope of resource, noting that they hope they might be able to increase sample size, or do a larger trial later on. The researcher is considering changing the study to a pilot/feasibility study in light of this.
2. The Committee queried whether there is a stratification on age and the severity of the mental status of the adolescents, noting that this is a concern with regard to the homogeneity of the group. The researcher responded that currently there is no stratification based on severity, partly due to sample size, but also because the criteria for entry into a CAMH service is a d moderate-severe mental health diagnosis, so there will not be enough of a range within their referrals to be able to stratify them further.
3. The Committee about the fidelity checklist, and the researcher noted that this is about ensuring adherence to TINT’s structured manualised programme and checking this across groups.

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 how compliance of parents’ home activities would be monitored. The researcher responded that informal monitoring is built into the programme, in the form of weekly practical problem solving that requires parents to use examples from their home activities during the week. The researcher noted that they could potentially include a post-programme questionnaire to ascertain parents’ compliance with the home activities. Please provide the post-programme questionnaire to the survey questionnaires to assess compliance of home activities.
2. The Committee queried how the researcher would deal with a missed session on behalf of a parent. The researcher responded that in the past, they have had 100% attendance from parents, which was supported by set agreements with parents which recommended that   
   they should not miss more than two sessions, and with space made available to do catch up sessions if need be. The Committee requested that the researcher update the protocol and PISs to include this, describing what the catch-up session would look like and that they can be run 1:1.
3. Please provide more detail about monetary compensations for participation in the study, in the study protocol.
4. The Committee requested that on the survey-questionnaire, greater transparency is provided around the meaning of the scoring.
5. The Committee noted a concern that mental health questions in the survey-questionnaires may enhance anxiety or distress. The researcher responded that they would ensure that there are measures in place to deal with this. This might include the provision of support service contact details as well as letting the participants know they can be in in touch with the research team.
6. The Committee noted that the study documentation references literature around consenting children, rather than the *National Ethical Standards for Health and Disability Research and Quality Improvement, 2019*, (NEAC Standards)*,* which contains standards for consenting children. The Committee noted that there is no Brightline age in NZ where participants are deemed competent to consent at age 16. The study has proceeded on basis that adults will be consenting on behalf of the child. The Committee noted that if a child has the capacity to consent, they should be enabled to do this. The Committee requested that the researcher read para 6.10 onwards of the NEAC Standards and amend their study documentation accordingly. Additional consent forms will need to be provided for young people who have the capacity to consent.
7. The Committee queried how the researcher would determine the capacity of adolescents to consent across the age range. Please provide guidance for this in the study documentation.
8. Please clarify in the study documentation what happens if a child wants to participate but the parent does not want them to.
9. The Committee noted that TINT has been used in in Northland, NZ, using an adapted version. The researcher responded that these adaptions are process related rather than content related, e.g., around incorporating tikanga. The Committee requested that the researcher include this information in the protocol.
10. Please include information about the advisory group and membership in the study protocol.
11. Please review the study advertisements to ensure they focus on providing information about the study rather than the TINT programme.
12. Please provide the demographic data that will be collected. Page 17 of the protocol doesn’t provide details other than stating it is ‘additional intake data’.
13. Please upload the emotion coaching diary.
14. Please provide the TINT manual and handouts.
15. Please provide an update on the Māori consultation from CCDHB Research Advisory Group – Māori. If this involves amending the PISCFs/PIS assent forms, these will need to be reviewed by HDEC.
16. As per para 12.15 of the NEAC Standards, the Committee requested that the researcher updates their data management plan (DMP), as follows:
    1. Clarify what happens to the comments and notes made on the fidelity checklists by the people running the TINT sessions and whether this is study data.
    2. Section 4 – it is not correct to state that all participants will have provided consent. Please amend to take into account the fact that some of the young people will be assenting and consent for them will be provided by a parent/caregiver.
    3. Section 7.2 – clarify what safety and screening results will be entered into the analysis data set.
    4. Section 7.3 – this is incorrect – only some of the data will be anonymous – the workshop data and the feedback. Anonymised data is different from de-identified data. Please amend.
    5. Section 8 – there are no sections 7.4 and 7.5. – please amend.
    6. NOTE: storage for young people is 10 years AFTER they have turned 16. Please amend.
    7. Section 11 – this does not make sense because there are no screening and safety tests
    8. Section 12 – does not align with the protocol and statements made elsewhere – please review and revise.

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

PISCF FOR PARENTS/CAREGIVERS ABOUT THE CO-DESIGN WORKSHOPS

1. Clarify that this study is for the obtainment of a PhD.
2. The second paragraph of page 1 does not make sense to talk about the care the parent/caregiver is receiving not being affected – please amend. This appears also on page 2 and page 3. Check the sense of the last sentence – there is a word missing.
3. Page 2 – please provide a brief description of the TINT programme
4. Page 2 – second to last paragraph – refer to ‘the’ study rather than to ‘your’ study.
5. The data section is not quite sufficient – it does explain about the anonymity of the workshop but it does not say who else will be in the workshop (other researchers) and that privacy cannot be guaranteed because other parents will also be in the workshop and may learn about the parent and the child’s problems. It is referenced in the CF but must be explained in the body of the PIS.
6. Explain that because of the anonymity, it will not be possible to allow for access or correction to information disclosed in the workshops. Explain that information will be recorded by field notes.
7. State where data will be stored.
8. Participants should also know whether something they say may be quoted – even if a name is not used, their child’s identity may be known to some people.
9. Clarify what kind of questions/comments might be asked about measure for part 2 given the anonymity.
10. The CF does not state if the researchers can contact them later by phone to follow up any questions or comment on any decisions made about measures for part two of the study (see page 3 of the PIS). Please clarify when this would occur.

INFORMATION SHEET AND ASSENT FOR YP ABOUT THE WORKSHOPS

1. Page 1 – provide a little bit more information about the TINT programme.
2. Page 1 – please reflect on the use of the term ‘teens’ because 3 of the age groups are not teenagers and those young people may feel excluded/mis-named.
3. Page 1 – it is not only up to the YP if they are too young to provide consent – their parents will have the decision-making power if the YP lacks capacity.
4. Page 1 – this statement will require amendment “Because you are under 16, if you do want to take part, we will also get consent from one of your parents/whānau. This means that we will also be giving them information about the study and making sure they are okay for you to take part.”
5. Page 2 – this statement requires amendment: “If you want to take part, you can sign the ‘assent form’ that also lets us get in touch with your parent or caregiver to make sure they are okay for you to participate. A parent or caregiver will also need to be available to bring you to the workshop and pick you up.” Please clarify why a parent/caregiver must be available to drop and collect.
6. Page 2 – please clarify what kind of questions they might ask after the workshop.
7. Provide information about privacy issues and data collection, results and publication.
8. The assent form will need to be changed and a consent form drafted for competent YP.

PISCF FOR PARENTS/CAREGIVERS ABOUT THEIR CHILD PARTICIPATING IN THE CO-DESIGN WORKSHOPS

1. Note comments above as relevant.
2. Requires amendment throughout to take into account that some YP will be able to consent for themselves.
3. Refer to other comments made about the PISCF for parents to attend the workshops because they apply here too (as relevant).
4. Page 2: this statement: “As this part of the study does not involve any involvement in your child’s care at CAMHS, there is no direct clinical benefit or risk of participating” is contradicted by the statements which follow which explain that the child might find it distressing to talk about mental health issues. Please amend.
5. CF: data about children must be kept for 10 years after the child turns 16.
6. The CF also needs to state that the child’s privacy will not be protected in the workshop and this needs to be explained in the body of the PIS.

PISCF FOR ADULTS FOR RCT

1. Please consider other comments in relation to the other PISs which apply here, as relevant.
2. Amend in relation to the young people who are able to give their own consent to answer questionnaires.
3. Refer to the Dryad Registry (details are in the DMP, section 8.9).
4. Please seek consent from participants to inform health practitioners with responsibility for their health care that they are taking part in your study.
5. Page 1 – check issues with description of ‘your care’ (throughout this PIS).
6. Page 2 – describe what the ‘measures’ are up front in more detail – how many questionnaires and what they are about and how long they will take to complete – this is especially important given the YP will be asked to complete some of the questionnaires. Describe which questionnaires adults will complete and which ones young people will be asked to complete. Potential participants cannot provide fully informed consent if they have no idea what type of questions they will be asked. Please clarify whether both arms of the RCT do the questionnaires.
7. Please clarify whether the third occasion for doing the surveys is 3 months (as stated in the protocol) or 8 weeks after the intervention (or control).
8. Please make it very clear that the questionnaires are not anonymous – they will use a unique study number.
9. Page 2 – explain what randomisation means
10. Page 2 – provide some detail about what the TINT programme involves and compare to what ‘usual care’ looks like. Inform how many other parents will be in the TINT workshops, as this has implications for confidentiality.
11. Break down the 2 components of the RCT into separate sub-headings under the heading “What will I have to do” – one sub-heading is about the questionnaires and the other would be about doing the TINT programme + UC or only UC.
12. Page 3 – In relation to the statement: “There is evidence from other research into this group that this can improve parent and child emotional regulation and reduce behavioural and mental health challenges”, please explain the research comes from Australia. Furthermore, clarify what is meant by ‘this group’ – do you mean ‘this programme’?
13. Page 3 – please balance the possible benefit statement with a statement that they may not find any benefit.
14. Page 3 – details of the questionnaires the young person will be asked to complete must be given together with the amount of time taken to complete, where they will complete them [the young person’s information sheet says it will be done online], the answers will be de-identified.
15. Provide a data section in this PIS. Refer to HDEC PISCF [template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc) for guidance.
16. CF – this needs considerable amendment having regard to the points made above in relation to the PIS and also in relation to other CFs, including, non-exhaustively, regarding choices on data use post withdrawal.

INFORMATION SHEET AND ASSENT FORM FOR YOUNG PEOPLE TO ANSWER QUESTIONNAIRES

1. Refer to comments on the adult PIS for the RCT which apply, as relevant, to this PIS. The assent form also needs amendment, and a consent form needs to be drafted.
2. Page 2 – please state the monetary amount of the voucher.
3. Please provide more information about what the TINT programme and the questionnaires involve.

**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 encouraged the researcher to resubmit to NTA, for the sake of continuity.

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| **12** | **Ethics ref:** | **2021 EXP 11197** |
|  | Title: | Mini S Feasibility Study |
|  | Principal Investigator: | Dr Andrew Holden |
|  | Sponsor: | Shockwave Medical, Inc. |
|  | Clock Start Date: | 29 September 2021 |

Dr Andrew Holden, Helen Knight and Andrew Hill 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 objective of this study is to assess the safety and performance of the Shockwave Medical Mini S Peripheral IVL System for the treatment of heavily calcified, stenotic peripheral arteries.

Summary of resolved ethical issues

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

1. The Committee highly commended the data tissue management plan (DTMP), checklist and appendix 1 that had been uploaded.
2. The Committee queried whether the PI participated in the cadaver trials for this system. The PI responded that he was not in the trial, but he has used [it] [ the study device]..
3. The Committee asked about the likelihood of adverse events. The researcher responded that this would be extremely unlikely. If this did occur, they would stop recruiting.
4. The Committee queried whether there is a NZ sponsor, and the researcher clarified that the ‘local’ sponsor is based in Australia.
5. The researcher noted that this is an international study, being reviewed by ethics committees in multiple jurisdictions, and that the sponsor has a preference for one protocol across the jurisdictions. The researcher queried whether the requested changes (described below) would need to be implemented into the international protocol. The Committee responded that their concern is for New Zealand participants, and that New Zealand participants needs to be part of the study documentation. The Committee advised that this could entail a NZ-specific appendix to the protocol.
6. Please report to Medsafe any SAE, SADE or USADE.
7. The Committee queried how many devices studies the researchers are doing concurrently and clarified that the researchers are satisfied that they have the capacity to run multiple studies concurrently.
8. The researcher explained that animal studies were not feasible because calcification is not replicated in animals.

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 one of the earlier trials of the shockwave system in NZ entailed a major adverse event (MAE), and asked the researcher to provide more information about this and whether this was attributable to the shockwave technology.
2. The researcher confirmed with the Committee that the study will start with two participants, who will monitored for 30 days to see if there are adverse events before other participants are recruited. Please update the study protocol to reflect this. The Committee discussed with the researcher that this may be achieved by way of formal letter of clarification or Protocol memo from the Sponsor.
3. Please formalise in study documentation that this is a multi-centre, international trial and clarify how this will operate, e.g. that there is communication between sites, in particular with regard to the study pause after the first two participants up to 30 days post-procedure.
4. The Committee noted that the insurance certificate covers Australian participants as well and depending on how many participants are split between Australia versus New Zealand, AUD 20 Million might not be sufficient cover for NZ participants. The Committee requested that the researcher provide more information on this to the Committee.
5. The Committee noted that the IB references biocompatibility results yet to be provided. Please provide.
6. The Committee queried the timing of consent, and whether potential participants would have a genuine opportunity for discussion with family. The researcher clarified that participants will have seen the PISCF before arriving at the hospital, up to a few weeks before the procedure. There will be a follow up phone call in this time to see if they have questions. Please build this into the study protocol.
7. In the data section of the protocol, do not overstate claims that individuals may be involved in the governance of their data.
8. Remove reference to questionnaires or interviews from the Auckland City Hospital DTMP.
9. Please remove inconsistencies in the data FUR section of the DTMP.
10. Please update outcome of the Māori Research Review Committee.

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

1. Please clarify in the PIS the withdrawal rights of the participant, including whether data collected up until point of withdrawal can be used.
2. Please clarify whether individual results are available or only the study results (the protocol says they are available upon request).
3. Please amend the statement: “This device has two main advantages when used in heavily calcified narrowings or blockages” – as this trial is designed to find out whether the device has the stated advantages.
4. Include information about the MAE when stating that shockwave technologies have been proven safe and effective in previous clinical studies.
5. Please note that standard animal testing has not been done with this study device.
6. In the table heading, rather than ‘not normal standard of care’, say ‘additional study procedures’ (or the like).
7. Highlight the specific risks relating to the study device, based on the information contained in the IFU manual, such as allergic immunologic reactions and device malfunction.
8. Please use the standard contraception wording from the HDEC PISCF [template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc).
9. Please replace the reference to the Southern HDEC.
10. Do not introduce new issues in the CF without first explaining them in the PIS.
11. On page 3 of the PIS, mention that the Rutherford Category will occur during screening.
12. Please inform the participant that target lesions revascularization occurs within the 12-month follow up period and that images acquired from the SOC are submitted to the Core Lab.
13. Please check the advocacy email address and HDEC email address and phone number for accuracy.
14. Please state where the lab is located in New Haven, Connecticut, USA, that will analyse the images, and whether this is the same as the Core Lab.

**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 2019, paras 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 2019,* *para 9.7*).

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

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

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| **Meeting date:** | 16 November 2021 |
| **Zoom details:** | TBC |

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 6.30pm.