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| **Committee:** | Northern B Health and Disability Ethics Committee |
| **Meeting date:** | 31 August 2021 |
| **Meeting venue:** | Online |

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| **Time** | **Item of business** |
| 11am | Welcome |
| 11.15am | New applications (see over for details) |
| 11.15 – 11.40am11.40 – 12.05pm12.05 – 12.30pm12.30 – 12.50pm12.50 – 1.15pm1.15 – 1.40pm1.40 – 2.05pm  | 21/NTB/217 Kate / Julie21/NTB/218 Helen / Devonie21/NTB/220 Dom / Julie*Break*21/NTB/222 Catherine / Devonie21/NTB/223 Kate / Julie21/NTB/225 Helen / Devonie  |
| 2.05pm | Meeting ends |

**Also in attendance:**

|  |  |
| --- | --- |
| *Member name* | *Member category*   |
| Mr Dominic Fitchett  | Lay |
| Ms Catherine Garvey  | Lay |
| Ms Julie Jones  | Non-lay |
| Mrs Kate O'Connor  | Lay (Chair) |
| Dr Devonie Waaka  | Non-lay |
| Mrs Helen Walker  | Lay |
| Mr Anthony Fallon | Lay (observing)  |

## Welcome

The Chair opened the meeting at 11am and welcomed Committee members, noting that this meeting was compiled of members across different Committees in order to be able to assist with the large influx of applications the HDECs have received.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

## New applications

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|  **1**   | **Ethics ref:**   | **21/NTB/217**  |   |
|   | Title:  | Patients with Type 1 Diabetes Using Hybrid Closed Loop System and Control at Home  |   |
|   | Principal Investigator:  | Dr Martin de Bock  |   |
|   | Sponsor:  | Medtronic New Zealand Limited  |   |
|   | Clock Start Date:  | 26 August 2021  |   |

Dr Martin de Bock and Alisa Boucsein 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.

Devonie Waaka declared a potential conflict of interest and the Committee decided that it was historic and not relevant to this study.

Summary of Study

1. Long-term health complications and increased mortality due to suboptimal glycaemic control are great concerns for patients with type 1 diabetes (T1D). Unfortunately, less than a third of patients meet glycaemic control targets recommended to prevent long-term complications. Provisional studies employing closed loop technology have shown a reduction in both hypoglycemia and hyperglycemia, as well as glycaemic variability. Previous studies have evaluated prototype versions of the Medtronic hybrid closed loop (HCL) insulin delivery systems in paediatric patients, as well as adolescents and young adults.
2. Medtronic has completed 7 phases in the HCL Feasibility Study (CEP 273) with a total of 71 subjects enrolled. In this Feasibility study, the closed loop system was stressed by artificially inducing sensor error as well as inducing physiologic stress such as exercise and administration of meals without bolus. The Feasibility study provided data, which was used to develop the device algorithm that is being tested in this study.
3. The investigational MiniMed 770G Insulin Pump that is being used in this study is equivalent in function to the MiniMed 670G insulin pump, with the exception of telemetry. While the MiniMed 670G insulin pump communicates on the basis of Tel-D (telemetry-diabetes) radio frequency (RF) technology, the MiniMed 770G pump contains BLE (Bluetooth Low Energy) RF communication, which allows for connectivity to patients’ smartphones, CGM transmitter and an BLE RF enabled blood glucose meter. The purpose of this study is to evaluate the safety and effectiveness of the HCL in patients with T1D in the home setting. A diverse population of patients with T1D will be studied. The study population will have a large range for duration of diabetes and glycaemic control, as measured by glycosylated haemoglobin (HbA1C).

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 even if a child provides assent or consent to participate in this study, that they cannot participate if their legal guardian does not also consent. This is because under the Care of Children Act (2004) a legal guardian must consent for provision of health procedures until age 16, and this study involves the provision of health services.
2. The Committee clarified with the researcher that participant identifiers such as name and date of birth will not be included in the CRF.

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 their concern regarding study participants not having continued access to the device system after the study had ended. The Committee requested that the sponsor ensures that the participants can keep and continue to use the device system after the study has ended, at no cost to the participant. Participants could either be donated the device to permanently keep, or allowed to keep it until a publicly funded equivalent to the device becomes commercially available. Components required to run the device (for example the CGM) should also be provided if not publicly funded. It was noted that as the device has been used by the participant, it will no longer have any commercial value.
2. The Committee noted a concern around equity of access to participate in the study due to requirement to access a computer, WiFi etc. The researcher noted that they would make options available to study participants, such as the provision of devices or the ability to come to the site rather than participate remotely, in order to ensure equal opportunity of participation. The Committee requested that the researcher builds this into their study protocol and PISCF.
3. Please provide a data management plan (DMP), ensuring that standards 12.15-12.15a of the *National Ethical Standards for Health and Disability Research and Quality Assurance*, 2019, have been met. Please refer to the [HDEC DMP template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/data-only-management-template-oct2020.docx) from the HDEC website.
4. The Committee queried whether all participants will receive a CareLink account and the researcher confirmed that all participants in the paediatric arm will receive an account. The Committee requested that the researchers build this into their data management plan (DMP).
5. The Committee noted that reasonable requests by the researcher to publish the results should not be declined by the sponsor, including negative results. The researcher responded that they will highlight the relevant part of the contract with the sponsor and submit to the Committee.
6. The Committee noted that the assent forms for child participants should not be based strictly on age and rather should be based on competency. Please ensure that child participants are provided with the assent form best suited to their level of comprehension.
7. Competent children under 16 should be treated as such and given the option to provide consent rather than assent.
8. The Committee noted that $32 reimbursement per study visit is grossly inadequate. The Committee requested that the reimbursement is enough to at least cover the costs of transport, parking etc.

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

PARENT/GUARDIAN PISCF

1. The Committee noted that the parent / guardian PISCF submitted was technical and long, and would need a fundamental revision to meet the standard required. The Committee requested that the researcher use the NZ HDEC [PISCF template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc) on the HDEC website.
2. Use a lay title.
3. Review for typos, grammatical errors and sentence structures.
4. Delete additional wording from the beginning of the compensation statement regarding health insurance, and the reference to NZ Medicines Guidelines (p18).
5. The Committee noted that the parents and legal guardians are part of the study so will need to be provided with a separate PISCF for their participation, or which distinguished what parents and guardians are being asked to do from what the children are doing, within the same document
6. GP notification of participation should be mandatory in a study of this nature. Amend accordingly (p4).
7. Include all NZ-specific consent clauses, for example regarding mandatory GP notification, optional receipt of study results, compensation arrangements in event of injury etc.
8. Inform the participant that you will be contacting their school and letting their teachers know.
9. Explain what happens if participants are already using an insulin pump with SAP and are in the control group (p2).
10. Give the approximate number of NZ participants.
11. State how long the required fast is and what to do if hypoglycaemia is experienced during the fast (p5).
12. Provide approx. visit durations. State how often questionnaires must be completed, and how long these will take on average (p13).
13. Provide frequencies if known for adverse events (p16).
14. Replace 'acetaminophen' with 'paracetamol'.
15. Re-write information section for clarity; use of 'personal data' to describe coded and non-coded information is unhelpful. Include the risks of sending data overseas and of privacy breach. Please use the wording provided on the HDEC template
16. The statement on page 3 “The 770G system mentioned above is approved by…” is a bit confusing as the HCL system was also mentioned above. Better to say “The 770G pump system (without the addition of the HCL system) is approved by…”
17. Throughout please correct “you” to “your child” where required. Ensure correct use of ‘you’, ‘you and your child’ and ‘your child’.
18. Do not say that “none of the procedures in this study are experimental” as the use of HCL is experimental.
19. Do not say “a urine or blood serum test to determine pregnancy will be performed.” – This makes it sound like they are meant to be pregnant. Better to say “a urine or blood serum pregnancy test will be performed”
20. Do not say “If your child passes all of the eligibility criteria”. It is better to say “if your child is found to be eligible for the study…”
21. On page 7, it is unclear what is meant by “office visit”. Elsewhere this is referred to as ‘clinic’. Correct throughout the table.
22. It is unclear why the follow up calls for visit 5 are listed as 6a, 6b, and 6c, whereas the follow up call for visit 4 is listed as 4a. Check and correct the visit schedule as appropriate.
23. Please note that the study can only be stopped for safety or because the product doesn’t work, not for commercial reasons. Please amend the reasons for stopping.
24. On page 27, under ‘how will the sponsor use my information?’, it is not clear if “Personal Data” only refers to the Medtronic CareLink system information or all 5 of the points listed. Clarify.
25. Better explain future research using participant data.
26. State how long data will be stored for (minimum 10 years after the age of 16).
27. Please ensure the consent form provides the opportunity to discuss with family.

ASSENT FORM (“12-15”)

1. Remove the reference to age range, as this form should reflect comprehension not age.
2. Proofread.
3. State that questionnaires need to be completed, how often and how long they will take, what happens at the clinic visits, and that data needs to be uploaded (and how often).
4. Include the statement from the 7-11 assent form regarding saying no despite parental consent.
5. Remove sexual activeness as a reason to pregnancy test. Rather, this should be based on menarche in order to avoid outing sexually active children in front of their parents.
6. Do not switch between referring to “mum, dad or the person taking care of you” and “parent/guardian”. Parent/guardian is preferable for this group.
7. Do not say “no one will be angry with you”. The doctors will not be angry, but you cannot predict the parents’ response.
8. On page 2, please clarify what is meant by a ‘blinded’ sensor. E.g. “*this means* that you will not be able to see that glucose readings”.
9. In the benefits statement on page 5, delete ‘their’ from the following sentence: “better treat their diabetes”.

ASSENT FORM (“7-11”)

1. Remove the reference to age range, as this form should reflect comprehension not age.
2. Include information about completing questionnaires and uploading data.
3. Do not switch between referring to “mum, dad or the person taking care of you” and “parent/guardian”. The former is preferable for this group.

ASSENT FORM (“2-5”)

1. Remove the reference to age range, as this form should reflect comprehension not age.
2. Say that it is fine to say no even if their parent says yes.
3. Provide space for assent (smiley / sad face) for participants judged capable of doing so.

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 the suggestions made by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 7.15 – 7.17).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Mrs Kate O’Connor and Julie Jones.

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|  **2**   | **Ethics ref:**   | **21/NTB/218**  |   |
|   | Title:  | 006 Efficacy study of GSK's investigational respiratory syncytial virus (RSV) vaccine in adults aged 60 years and above.  |   |
|   | Principal Investigator:  | Dr Dean Quinn  |   |
|   | Sponsor:  | PPD  |   |
|   | Clock Start Date:  | 05 August 2021  |   |

Dean Quinn and Aurelie Olivier 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. GSK is developing a new RSV PreFusion protein 3 Older Adult (RSVPreF3 OA) investigational vaccine against respiratory syncytial virus (RSV)-associated (subtypes A & B) disease in adults ≥60 years. The vaccine development is in phase 3.
2. The current study will assess the efficacy of a single dose of the RSVPreF3 OA investigational vaccine in the prevention of reverse-transcriptase polymerase chain reaction (RT-PCR)-confirmed lower respiratory tract disease (LRTD) caused by RSV A and/or B in adults > 60 yrs. In addition, the safety and immunogenicity and the vaccine cross-protection against RT-PCR-confirmed LRTD caused by human metapneumovirus (hMPV) will be evaluated.
3. The study is phase 3, randomized, observer-blind, placebo-controlled multi-country study to demonstrate the efficacy of a single dose of GSK’s RSVPreF3 OA investigational vaccine in adults aged 60 years and above. Participants will receive either the RSV Vaccine or placebo.
4. The study has 2 Parts:
5. Part 1 with 4 parallel groups (randomised 1:1 however the RSV vaccine will use 3 different Lots).
6. Part 2 with 2 parallel groups, (randomised 1:1) which will be initiated when the vaccine lots for Part 1 are no longer available at the study sites.
7. Duration of the study is approximately 2.5 to 3 years per participant in SH (up to at least 2 consecutive RSV seasons).
8. The timing of the study activities is linked to the RSV seasons & divided in 2 parts:
	1. General study activities for all participants. All Participants will receive a single dose of RSV vaccine or placebo at Visit 1 & return at Visit 2 after 1 month. There are regular phone contacts during that RSV season and during the next RSV season. They will also return for a visit before and after the second RSV season.
	2. Activities only if a participant has cold-like symptoms. During the sttudy participants are asked to complete activities if they develop 2 or more cold-like symptoms and to contact and return the study site for assessment.

Summary of resolved ethical issues

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

1. The Committee requested that the researcher use more lay-friendly language in the application form for future submissions.
2. The Committee queried whether it is three or 12 countries involved in this study, as the application alludes to both. The researcher responded that the study is running in both the Northern and Southern hemispheres. The reference to participants in three other countries refers to the Southern Hemisphere component of the study, whereas the 12 countries includes both Northern and Southern hemispheres.
3. The Committee queried the process in place for if anxiety or depression was indicated in participant answers to the questionnaires. The researcher responded that questionnaires would be reviewed on the day they were filled in and concerning results would be referred on to the GP for follow up.
4. The Committee noted that question r1.6 of the application form states that the sponsor has the right to close the study at any time at their sole discretion. The Committee clarified that this is not the case – the study cannot be stopped for commercial or administrative reasons, and the sponsor representative agreed.
5. The Committee noted that many of the documents that had been uploaded with the application were out of scope for committee review, including a blank thank you card, eligibility criteria card for use by investigators, blank pocket folder, adjudication charter final draft with tracked changes etc. These documents have not been reviewed or approved by the Committee.
6. The Committee queried who the newsletter written in Latin is intended for, noting that it cannot be approved without knowing who it is going to or what it is for. The researcher responded that this is a site-facing document. The Committee noted that this is out of scope of HDEC review.
7. The Committee noted that in one part of the application, it was stated that samples will be destroyed if no longer needed for the study, and that elsewhere it stated that the default is for samples to be stored for 20 years. The researcher clarified that study follow up could go on for 20 years. Samples might also be kept if consent for FUR has been obtained.
8. The Committee queried the amount of compensation for travel. The researcher responded that this would be around $100 per visit.
9. The Committee noted that caregivers do not consent to participate because they are just helping out rather than actively participating in the study.
10. The researcher confirmed that caregivers will be provided with gloves to perform the nasal swabs.

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 a data privacy breach would be notified to the participant. The researcher responded that this would follow site policy, to determine whether or not the participant should be notified. The researcher confirmed that the site’s default policy is to inform the participant of a data privacy breach unless there was a significant reason not to. Please clarify this in the data tissue management plan (DTMP).
2. The Committee noted that the data management response to r.2.1.1 states that sponsors, auditors etc will have access to health information on site before the study has commended. The Committee noted that this is not acceptable – no identifiable health information should be provided before participants have signed informed consent. Please clarify in the DTMP.
3. In the Health Care Provider letter, please make it very clear that the provider needs to get agreement from the patient prior to referring patients to the researcher. Please also include important concomitant medication restrictions so that the primary health care provider is aware of these.
4. In the Dear Patient letter, please explain who the letter is being sent from.
5. The Committee requested that all advertising states that the vaccine is investigational.

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

MAIN PIS

1. Please include the approximate number of NZ participants.
2. In the data section, please include the risk of sending data overseas and the risk of privacy and confidentiality breach. Please see the standard text in the [HDEC PISCF template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc) for guidance.
3. Please make clear in the body of the PIS that the GP will be informed of study participation and any clinically significant abnormal study results. This is not optional.
4. Please clarify whether or not participants can reveive the COVID-19 vaccine or other approved vaccines during the study.
5. Please clarify that there are two different types of nasal/nostril tests with different levels of invasiveness, and that one will be done by the participant and other by a clinician.

INFORMED CONSENT MODEL TEMPLATE INFORMATION CAREGIVERS SHEET

1. Please clarify that involvement is optional.
2. Please clarify what will happen if the caregiver does not want to help, or wants to pull out during the study, and how this will affect the participant’s involvement in the study.
3. Please provide the study schedule so that the caregiver knows what their burden is.
4. Please clarify the risk of some of the procedures they will be asked to do, e.g. swabbing.
5. Please clarify that the travel reimbursement will be given to the participant and not to the caregiver.
6. Please clarify whether or not the caregiver’s name will be stored in the study medical records.

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee.
* Please update the Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 7.15 – 7.17).*

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

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|  **3**   | **Ethics ref:**   | **21/NTB/220**  |   |
|   | Title:  | The C-CAT Study  |   |
|   | Principal Investigator:  | Professor Cindy Farquhar  |   |
|   | Sponsor:  | The University of Auckland  |   |
|   | Clock Start Date:  | 19 August 2021  |   |

Professor Cindy Farquhar and Karyn Anderson 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 is a multicentre, randomised, placebo-controlled clinical trial. Participants with recurrent implantation failure, defined as 2 or more embryo transfers without a clinical pregnancy, who are receiving an IVF cycle or frozen embryo transfer will be randomised to 1 of 2 intervention arms, combined adjuvant therapy or placebo. In addition to their standard IVF treatment, those randomised to the combined adjuvant therapy arm of the trial will receive a package of 3 medications: Aspirin (taken from day 1 of stimulation to 13th week of pregnancy), Prednisone (taken 3-5 days before embryo transfer for 7 days), and Augmentin (taken 3-5 days before embryo transfer for 7 days). Those randomised to the placebo arm will receive identical appearing placebo medications to be taken in the manner outlined for the active medications. The primary outcome is live birth rate. Secondary outcomes include: biochemical pregnancy rate, clinical pregnancy rate, miscarriage rate, rate of serious adverse events (including allergy, congenital anomaly, death), and compliance to the trial medication protocol.

Summary of resolved ethical issues

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

1. The Committee queried the recruitment process for a couple who has failed two implantations, whether in standard of care they would usually go on a list for a third implantation and whether this is publicly funded. The researcher responded that public funding is available if they meet the criteria and if they still have embryos available.
2. The Committee queried the gap between second and third implantations and the researcher responded that the participant can go straight into it upon their next menstrual cycle.
3. The Committee clarified with the researcher that the participants are willing to make a third attempt at implantation before the research team approaches. This will ensure that the offer of participation will not influence the decision of couples to have another go at implantation.
4. The Committee confirmed with the researcher that participation will not disadvantage non-participants by bumping them down the list for having the implantation.
5. The Committee queried whether reference to the ‘Colorado Protocol’ in the study poster will be understood by prospective participants. The researcher responded that this is understood by people in the fertility world and has significant name recognition.
6. The Committee noted that the scientific peer review suggested an interim analysis, which the researchers have not implemented into their study protocol. The researchers clarified that this is because it is generally frowned upon in the clinical scientific world, as it often influences the behaviour of the research team and can create bias with future analyses. The researchers noted that they would be severely criticised if they implemented an interim analysis. The researchers noted that they have implemented the core outcomes set.
7. The researcher clarified that they have a safety analysis.
8. The researcher clarified that there are no extra study visits beyond standard-of-care.
9. The Committee queried where the electronic consent is held, and how access to this identifiable info is being limited. The researcher responded that it is being held on the REDCap database, and that only people authorised for this study will have access. It will only be accessible at the locality that the patients are at.
10. The researcher clarified that there is only one treatment phase for this study – participants can only be in the study once.
11. The Committee queried what data would be obtained through the participant treatment questionnaire and how useful it would be for the study, as it does not appear to be study specific. The Committee noted that it is a standard questionnaire that was developed separately from this study and may not be helpful to 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 requested a data management plan (DMP), including information about the life cycle of data and data sharing from clinics. Please refer to the [DMP template on the HDEC website](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/data-only-management-template-oct2020.docx) for guidance. Para 12.15, *National Ethical Standards for Health and Disability Research and Quality Improvement*, 2019.
2. The Committee queried the researcher’s response to r.2.1.1. about data being entered and retained in the REDCap database for people who do not sign informed consent, and asked the researcher to confirm that this is not the case, as data should not be collected and stored without consent. The researcher responded that it is standard at the University to collect and retain screening data without consent. The researcher clarified that the data retained would include length of infertility. The Committee responded that if they would like to do this for their study, and there is a scientific rationale for it, this would require a waiver of consent, as per paras 7.46-7.48a of the *National Ethical Standards for Health and Disability Research and Quality Improvement*, 2019. Please build this into your data management plan.
3. The Committee requested that the researcher revisit their compensation statement in relation to their study, as it is very difficult to obtain ACC cover, especially for injury in utero. Please consider how this relates to the disclosure of foreseeable and unforeseeable risks.

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

1. Please update the PIS to include all the relevant sections and information referred to in the HDEC [PISCF template on the HDEC website](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc), especially in regards to the consent process, how participation differentiates from standard of care, data collection, use and storage and time commitments for participation in the study.
2. Please include the PI phone number.
3. Please include a reference to HDEC review and ethical approval.
4. Please use a different term for dummy pills, such as ‘inactive pills’.
5. Please better explain what ‘GI upset’ is.
6. Please clarify that you will be collecting information about the rate of serious adverse events including allergy, congenital anomaly, death etc.
7. Please clarify that identifiable information held on the REDCap database will only be accessed by the research team at the locality that the patients are at.
8. Collecting information about the child after birth requires parental consent after the child is born. Please provide a PISCF for this, referring to the pregnancy follow up child PISCF HDEC [template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/hdec-pregnancy-follow-up-child-participant-information-sheet-consent-form-template-jul20.docx) on the website for guidance. This will not be required if all you are collecting is pregnancy outcome, and the consent statement about follow-up data about the child can be removed
9. Please reconsider the statement about keeping a close eye on birth defects that may occur as this is not plausible.
10. Please consider including a patient diary for the dosing.
11. Please be clear that the Colorado protocol treatment will not be available unless you are part of this study.

Decision

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

1. Please address all outstanding ethical issues, providing the information requested by the Committee.
2. Please update the Participant Information Sheet and Consent Form, taking into account the suggestions made 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 Mr Dominic Fitchett and Ms Julie Jones.

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|  **4**   | **Ethics ref:**   | **21/NTB/222**  |   |
|   | Title:  | Evaluating method for determining lymphatic composition via central venous sampling.  |   |
|   | Principal Investigator:  | Professor John Windsor  |   |
|   | Sponsor:  | University of Auckland  |   |
|   | Clock Start Date:  | 26 August 2021  |   |

Jim Li 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 overall aim of the project is to evaluate a new technique to sample thoracic duct lymph without relying on direct surgical cannulation. This will allow for a less invasive and more readily available method to determine compositional changes in lymph in patients with critical illness.
2. The study involves recruiting surgical patients with nasogastric tubes, venous central lines and peripheral lines in CVICU (cardiovascular intensive care unit) at Auckland City Hospital. Post-elective cardiac surgery, ingestion of lipid rich cream (orally or via nasogastric tube) will promote production of lymph and lymphatic markers such as Apolipoprotein ApoB48 or Triglyceride levels, the increase of which can be detected in blood. Central venous catheters can then be used to sample blood from the Internal Jugular or Subclavian vein upstream and downstream of where the thoracic duct drains into the vein. The blood will then be examined for concentration of lymphatic markers, and differential composition upstream vs downstream will be compared to determine contribution by thoracic duct lymph. Blood sampling will be done at different points in the respiratory cycle to help ascertain period of maximal lymph flow.
3. The endpoint of the study is to show that this technique is effective in measuring differences in blood concentration due to lymphatic contribution, and that blood sampling can then be used to monitor compositional changes in lymph with critical illness.

Summary of resolved ethical issues

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

1. The Committee asked about the recruitment process for this study. The researcher responded that they are planning on recruiting elective cardiac surgical patients before they have surgery. They will be asked by their clinician if they are interested in participating in the study before being referred to the researcher for recruitment. Participants will have time to take the information sheet away and discuss it with their family before making a decision about participation.

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 whether participation in the study would require further sedation beyond what is required for the standard of care surgery. The researcher responded that this is not the case – the research team will take the samples whilst the participants are still sedated post-op, in PACA. They will still be asleep and on the ventilator. The reason for taking the samples whilst the participant is sedated is because the samples are timed with their breathing, which is easier when they are on ventilation. There is a contingency plan in place for if a participant wakes up before the samples have been taken. The Committee requested that information of this is included in the protocol and PIS.
2. The Committee noted that the cream that is given to participants includes dairy. Please update the study protocol and PIS to include an exclusion criterion for people who cannot, or do not wish to, consume dairy products.
3. The Committee requested that the researcher provides a data and tissue management plan (DTMP). Please see the [HDEC DTMP template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/hdec-data-tissue-management-template-oct2020.docx) for guidance, and tailor it to your study. This can be incorporated into your protocol or submitted as a standalone document.
4. Please update the study protocol to include provisions for monitoring and reporting adverse events.
5. Please update the protocol to discuss the informed consent process for both the study and the optional future unspecified research. Please clarify that eligibility criteria is limited to those who are able to provide informed consent.

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

1. Please ensure that any study specific procedures and associated risks are included in PIS, for example information about checking correct catheter placement, catheter removal, nasogastric tubes.
2. The Committee noted that the study protocol has been updated from the version submitted to HDECs. The Committee requested that these changes are updated in the PIS/CF.
3. Please make clear in the main PIS that there is no genetic testing.
4. If you would like to contact participants in the future for additional research, please notify them of this in the PIS and provide an optional tick box for it in the CF.
5. Please consider including pictures of the lines in the neck in the PIS, to help inform participants.
6. Please inform the participant and provide a mandatory consent clause for contacting the GP.
7. Please remove green text on page 7 of the main PIS.

Decision

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

1. Please address all outstanding ethical issues, providing the information requested by the Committee.
2. Please update the Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee. (National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 7.15 – 7.17).

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

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|  **5**   | **Ethics ref:**   | **21/NTB/223**  |   |
|   | Title:  | Telehealth-delivered health-promoting interventions for autistic children  |   |
|   | Principal Investigator:  | A/Prof. Laurie McLay  |   |
|   | Sponsor:  | University of Canterbury  |   |
|   | Clock Start Date:  | 26 August 2021  |   |

Associate Professor Laurie McLay was present via videoconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The study has four aims:
2. To explore the efficacy of telehealth-delivered behavioural treatment methods for eating/feeding or toileting problems in children on the autism spectrum.
3. To identify the essential components of effective telehealth interventions for addressing eating/feeding or toileting problems in children on the autism spectrum.
4. To identify whether the telehealth approach is seen by parents/guardians to be culturally responsive, acceptable, and beneficial to themselves and the child.
5. To assess the impact of the treatment programmes on the children’s daytime behaviour and symptoms of autism spectrum disorder (ASD), and parent/guardian and child wellbeing.
6. The researcher team aim to recruit a minimum of 30 children who meet the following criteria:
7. a diagnosis of ASD
8. between 2 and 5 years of age
9. parent-reported eating/feeding or toileting problems; and
10. no medical condition or medication use that may interfere with behavioural treatments.
11. The research team have established channels for recruitment based on their current research programmes.

Summary of resolved ethical issues

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

1. The Committee noted that this study is about young children who show signs of or have a diagnosis of ASD. The Committee asked how questions of eating and toileting would be different to the average young child who is slow to go to the toilet or is afraid of the toilet. The researcher stated that there is a lot more resistance around some behaviours associated with toileting, such as sitting, complying with instructions etc. Similarly, in terms of feeding, there is resistance to complying with sitting at the table and there is a limited repertoire of food that children with ASD will eat. A reason why this study includes such young children is because there is evidence to suggest that it is important to intervene at young stages particularly in regards to feeding and toileting. The researcher noted that the toileting study will likely involve slightly older children than those in the feeding study.
2. The Committee noted that recruitment will be through various parenting groups the research team is already connected with, autism advocacy groups, and a flyer that people can use to contact the research team if interested. The Committee had no concerns with study recruitment.
3. The Committee noted that the Zoom meetings will not be recorded.

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 content, modules, and training that parents/guardians will interact with will all be put on a website. The researcher confirmed this and advised that the content has been written up but not uploaded yet. Please provide copies of all content that will be uploaded to the website, for the Committee to review.
2. The Committee asked if a family can be involved in more than one of the three studies (feeding, toileting, and sleeping). The researcher confirmed this but stated that involvement in all three studies at the same time is not recommended. Please put this information in the Participant Information Sheet to inform participants that just because they are in one study, does not exclude them from participating in another study later on.
3. The Committee asked what the purpose of randomising baseline lengths is. The researcher stated that within single case research designs, it is a feature that helps to maintain the integrity of the research. Please provide an explanation in lay language in the Participant Information Sheet with the reason as to why participants are being randomised to different lengths. The Committee also suggested removal of the reference to ‘flipping a [two-sided] coin’ given there are three baseline lengths (five, 10, or 15 days).
4. The Committee noted that internet access is required for study participation. The Committee asked how families without internet will be able to participate. The researcher advised that the study budget may account for this and there may be internet chips/data packages available for participating families. The study web-based content is also accessible via mobile phone browser. Please include this information in the recruitment flyer and Participant Information Sheet.
5. The Committee noted that the data management plan is not described well in the protocol. The Committee referred the researcher to the HDECs [Data Management Plan template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/data-only-management-template-oct2020.docx) and advised that the template be used to work through distinguishing identifiable from coded data, who has access to what, in what form data is kept, how long stored data is stored for, how data will be destroyed etc. A clear governance framework for the study data will be helpful.
6. The Committee noted that there is no indication of how long study data will be kept. Please review the [Health (Retention of Health Information) Regulations 1996](https://www.legislation.govt.nz/regulation/public/1996/0343/latest/DLM225616.html) to see what is applicable to the study, then provide information about the timeline of retention of study information in the Participant Information Sheet.
7. The Committee referred to r.2.4.1 of the application form which states that some identifiable information will be stored online. The researcher clarified that no identifiable information will be stored online. Please ensure this is made clear in the study documentation.
8. The Committee asked if any meta data will be collected from the website. The researcher confirmed that they will look at analytics on the backend of the website in terms of the number of times people access it and how much time is spent on the website. Please detail this in the data management plan and Participant Information Sheet.
9. The Committee noted that the children’s assent forms state that if children decide not to participate, ‘no one will be angry with you’. Please amend these statements to say that, ‘the researchers will not be angry with you’ if children decline to participate.
10. The Committee requested that in the children’s assent form, the person who ‘knows a lot’ about helping children eat i.e., ‘the expert’, be described as the expert throughout the document, to avoid confusion.
11. The Committee suggested that the term ‘your adult who takes care of you (your adult)’, using ‘your adult’ thereafter, be used throughout for children’s assent forms to make it easier to understand and less wordy.
12. The Committee noted that the consent form for the children’s assents may be difficult to understand (especially for 2 to 5-year-olds) due to contradictory instructions on ticking boxes versus putting an ‘x’ in the boxes. The Committee suggested using sad face and smiley face pictures for children to circle instead.
13. Please replace the picture of the child eating from the toileting assent form.
14. The Committee noted that the adult Participant Information Sheet and Consent Form states that ‘we are inviting you’ to take part in the study, but it should state, that ‘we are inviting you and your child’. Please use the appropriate wording throughout the form.
15. The Committee noted that at a.1.6 of the application form, the research team has a safety plan in place should the assessments or conversations indicate the need for mental health support. However, this is not discussed in the Participant Information Sheet. If there is a safety plan, please put information about this in the Participating Information Sheet.
16. The Committee noted that at a.1.6 of the application form, the research team ‘will contact the child’s lead medical carer’ if in doubt on whether a child has a physical or medical condition that impacts their feeding or toileting (exclusion criteria). Please clearly state in the Participant Information Sheet and Consent Form that the child’s general practitioner may be contacted for this reason.
17. The Committee noted that the study involves a period of group coaching via Zoom. Please provide some guidance for participants in regards to etiquette and confidentiality required for the focus groups and information discussed within them.
18. The Committee noted that Māori consultation recommended the need for koha for participating whānau. If koha will be offered to Māori participants, this should also be offered to remaining participants to be fair to all who participate.

The Committee requested the following changes to the Participant Information Sheet and Consent Form, in addition to the changes already referenced above:

1. Please change the title of the main Participant Information Sheet from the word ‘caregiver’ to ‘guardian’. Unless the person is an official guardian, a caregiver cannot consent for this study. The Committee noted that this was also a non-standard condition for approval of the researcher’s sleeping study.
2. Please make clear that there are 30 participants across both studies.
3. Please include information about how long each module will likely take.
4. Under ‘What are the possible benefits of this study?’ please also state that there may be no benefits as a result of participation in the study.
5. Please include the wording around eligibility for compensation as a result of injury during the study (Accident Compensation Corporation). This wording is available in the HDECs [Participant Information Sheet and Consent Form template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc).

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 and Assent Forms, taking into account the suggestions made by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 7.15 – 7.17).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Ms Kate O’Connor and Ms Julie Jones.

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|  **6**   | **Ethics ref:**   | **21/NTB/225**  |   |
|   | Title:  | A Biosimilar Study to Compare BP11 with EU-Xolair® and US-Xolair® in Healthy Males  |   |
|   | Principal Investigator:  | Dr Leanne Barnett  |   |
|   | Sponsor:  | Syneos Health  |   |
|   | Clock Start Date:  | 26 August 2021  |   |

Dr Chris Wynne, Dr Leanne Barnett, Courtney Rowse, Sharmin Bala, and Tessa Moncrieff 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. Omalizumab is used for the treatment of allergic asthma, chronic rhinosinusitis with nasal polyps, and chronic idiopathic urticaria (sudden onset of hives and itching), and is approved and sold under the brand name ‘Xolair’. The Sponsor has developed a drug similar to Xolair, called ‘BP11’. The study aims to investigate that BP11 is similar to US licensed Xoliar (US-Xolair) and EU licensed Xolair (EU-Xolair).
2. The study will also compare the drug safety, how well it is tolerated, the levels of the drug in the blood at different times, and the body's immune response (in terms of producing antibodies against the drug, called antidrug antibodies or ADAs).
3. This study will be conducted at New Zealand Clinical Research in Auckland and Christchurch and comprise up to approximately 165 healthy male participants (55 per treatment arm). Each participant will be randomly assigned to one of three treatment arms in a 1:1:1 ratio to receive a single 150 mg subcutaneous (SC) dose of either BP11, EU-Xolair, or US-Xolair. The study requires a three-night inpatient stay and 16 outpatient visits. The results will be used to further develop BP11 as a biosimilar to Omalizumab.

Summary of resolved ethical issues

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

1. The Committee noted the current outbreak of COVID-19 in New Zealand and Alert Level 3 requirement except for Auckland in Level 4. The Committee asked if, after approval, the study would go ahead in Christchurch but not in Auckland. The researchers confirmed this, but also noted that part of this will depend on social distancing requirements at the Christchurch site.
2. The Committee discussed the advertising used for the study. The Committee was satisfied with the advertisement, however, asked that the sum participants will be paid for participation in the study is not made as a headline or main aspect of the advertisement.

Summary of outstanding ethical issues

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

1. The Committee referred to section 13 of the Data and Tissue Management Plan (DTMP) and noted that it contradicts r.3.12 of the application form. The application form states that participants can request that already collected tissue be destroyed with no further analysis undertaken, while the DTMP and PISCF state tissue will continue to be used for mandatory study purposes. Please check what is intended.
2. The Committee requested that Section 4 of the DTMP be amended to address additional consent for optional secondary purposes.
3. The Committee requested that future use of tissue is addressed in section 8.4 of the DTMP. Currently, this section only refers to data.
4. The Committee noted that there is limited information in section 7.2 of the DTMP around remote monitoring. Please clarify who has remote access and to what, and how this is managed (for example, limited access, no downloading/copying data etc.).
5. The Committee noted that the DTMP (section 8.4) and Participant Information Sheet reference data being sent to Europe, India, and the United States. The sponsor is in India, however, no description about Europe and the United States is provided. Please provide this.
6. The Committee noted that information may be gathered from participants’ general practitioners’ (GPs) records. Please state clearly in the Participant Information Sheet and Consent Form that the research team will contact GPs and why.
7. The Committee asked if participants can get the government approved COVID-19 vaccine during the study. The researchers stated that the protocol has been updated and participants can get vaccinated after day 15 of the study (exclusion criterion #8). The Committee requested this information be included in the Participant Information Sheet.

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

1. Please explain what the ‘first four days of the study’ means in terms of lifestyle restrictions, i.e. whether it is the first four days of screening, first four days after admission to the unit, or after dosing.
2. Please amend the statement on page 7 (‘Standardised means…due to its relationship with metabolism of investigational product’) so that it is written in plain lay language.
3. Please remove duplicate information. Section 5.2 is unnecessary as it is already stated under the risk section in section 6.3. Please also delete the second paragraph of section 1.3 or the ‘Ownership rights’ paragraph in section 6.3.
4. Please review section 7.2 – the second and third bullet points do not apply to this study, which is non-therapeutic and does not assess efficacy.
5. Please amend the clause in the Consent Form that discusses the participant becoming pregnant, as only males are being enrolled in the study. Please limit the statement to refer to partners only.

Decision

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

* please address all outstanding ethical issues, providing the information requested by the Committee
* please update the Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 7.15 – 7.17).*

## General business

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

The meeting closed at 2.05pm.