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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 17 August 2021 |
| **Meeting venue:** | ONLINE - Zoom Meeting |

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| **Time** | **Item of business** |
| 1.00pm | Welcome |
|  | Confirmation of minutes of meeting of 20 July 2021 |
| 1.20pm | New applications (see over for details) |
| 1.20-1.45pm  1.45-2.10pm  2.10-2.35pm  2.35-3.00pm  3.00-3.20pm  3.20-3.45pm  3.45-4.10pm  4.10-4.35pm  4.35-5.00pm  5.00-5.20pm  5.20-5.45pm  5.45-6.10pm  6.10-6.35pm  6.35-7.00pm | 21/NTA/133 Karen / Helen  21/NTA/144 Kate / Catherine  21/NTA/152 Sotera / Catherine  21/NTA/131 Michael / Helen  Break  21/NTA/130 Sotera / Dom  21/NTA/135 Kate / Dom  21/NTA/136 Sotera / Helen  21/NTA/138 Michael / Catherine  Break  21/NTA/142 Karen / Sarah  21/NTA/154 Kate / Helen  21/NTA/132 Karen / Catherine  20/NTA/75/AM06 Michael / Sarah |
| 7.00pm | Meeting ends |

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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 | Present |
| Mrs Kate O'Connor | Lay (consumer/community perspectives) | 29/01/2020 | 29/01/2021 | Apologies |
| Mrs Helen Walker | Lay (consumer/community perspectives) | 22/05/2018 | 22/05/2020 | Present |
| Dr Kate Parker | Non-lay (observational studies) | 11/02/2020 | 11/02/2023 | Present |
| Ms Rochelle Style | Lay (ethical/moral reasoning) | 14/06/2017 | 14/06/2020 | Apologies |
| 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 |
| Dr Michael Meyer | Non-lay (health/disability service provision) | 11/02/2020 | 11/02/2023 | Present |
| Mr Dominic Fitchett | Lay (the law) | 05/07/2019 | 05/07/2022 | Present |
| Dr Sarah Gunningham | Lay (other) | 05/07/2016 | 05/07/2019 | Present |

## Welcome

The Chair opened the meeting at 1pm and welcomed Committee members, noting that apologies had been received from Kate O’Connor and Rochelle Styles.

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 20 July 2021 were confirmed outside of the meeting.

## New applications

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| **1** | **Ethics ref:** | **21/NTA/133** |
|  | Title: | Skyscraper03: GO41854 Tiragolumab + Tecentriq vs Durvalumab in Unresectable Stage III NSCLC |
|  | Principal Investigator: | Dr Laird Cameron |
|  | Sponsor: | Roche Products New Zealand Ltd. |
|  | Date submitted: | 22 July 2021 |
|  | Clock Start Date: | 05 August 2021 |

Dr Laird Cameron, Kerry Walker and Bronwyn Gale 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.

Kate Parker and Karen Bartholomew declared a potential conflict of interest and the Committee determined it was historical and decided to allow them to participate in the discussion.

Summary of Study

1. This is a phase III study which enrols patients with locally advanced, unresectable Stage III non-small cell lung cancer (NSCLC) who have had concurrent platinum-based CRT and have not yet progressed. This study randomises these patients 1:1 to receive 13 treatment cycles of either atezolizumab plus tiragolumab or durvalumab alone. Participants will be assessed during this treatment for disease progression and then followed up for 48 months following the end of treatment to assess survival.

Summary of resolved ethical issues

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

1. The Committee was satisfied that arm of the study was of potential benefit to potential participants after discussion with the researcher.
2. The Committee stated they were comfortable with a shortened information sheet for the treatment continuation.
3. The Committee noted the potential participant burden of all the PISs and queried if the researchers have a schedule for presenting these rather than all at once. The researcher responded that the patients have time between receiving information and talking it through with the researchers. There are some that are presented in the event they are needed; however, most are provided upfront if they are interested in 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 queried if it was ethical for pre-screening tissue sampling that is mandatory if a participant wishes to be on the study gets sent for Future Unspecified Research (FUR). The current wording in the pre-screening participant information sheet (PIS) reads as blanket FUR that is not optional, and not everyone who undergoes pre-screening would then go on to the study but would still have their tissue used. The Committee noted their concern that this was not-optional FUR without separate consent as required by the *National Ethical Standards for Health and Disability Research and Quality Improvement* *2019* para 14.48.
2. The Committee queried why the Whole Genome Sequencing (WGS) consent is separate to the Research Biosample Repository (RBR) consent, as the RBR consent is very broad and includes genetic testing.

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

1. Please clarify upfront in the tissue pre-screening PIS/CF the purpose and the timing of the tissue samples being taken and what kind, and why, as this is not being done as part of standard of care.
2. Data sections across PISs do not describe what data accompanies samples. Please review and clarify what data is going with the tissue in each respective PIS.
3. Please clarify upfront in the RBR PIS that you are asking participants for a new sample.
4. Please update the RBR PIS to include a data section and include genetic disclosure risks in the privacy section.
5. Please include in the RBR CF a line item that acknowledges they understand that genetic testing will be done on their tissue.
6. Please clarify in the WGS PIS why there are no return of results.
7. Please ensure the WGS and RBR PISCFs are compliant with the *National Ethical Standards for Health and Disability Research and Quality Improvement* *2019* paras 7.58 and 14.27-14.41.
8. Please consider the phrasing in the Continuation PIS “Your total treatment period will last for up to 13 cycles or until your disease worsens” to “worsens again” to clarify, as this PIS is for participants with disease progression.

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

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

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| **2** | **Ethics ref:** | **21/NTA/144** |
|  | Title: | Impact of parental brain injury on their children's quality of life |
|  | Principal Investigator: | Mrs Audrey McKinlay |
|  | Sponsor: | University of Canterbury |
|  | Date submitted: | 04 August 2021 |
|  | Clock Start Date: | 12 August 2021 |

Audrey McKinlay and Lihini Mendis 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. All young people (age 8 - 18 years) who have a parent currently receiving treatment through the Laura Fergusson Trust for a brain injury event, and their uninjured parent, will be invited to participate. Child participants and uninjured parents will be asked about the changes they have experienced in their family following the TBI event, and the impact that these changes have had on their daily lives. Uninjured parents and participants aged 8-18 will complete a semi-structured interview and three questionnaires (Paediatric Quality of Life Inventory, the Conners – 3 and the Revised Child Anxiety and Depression Scale). The aim of the study is to develop programmes and improve outcomes for young people living with an adult who has a brain injury.

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 was lacking some detail e.g., background, literature review, aims or objectives, analysis plan, risk management plan, detail about how power is calculated, how concerning findings will be responded to, what pilot questions are being answered, etc. *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019,* paras 9.7& 9.8*).*
2. The Committee noted that the data is de-identified, not anonymised. This means return of results is possible and incidental findings could be acted on. Please update the study documentation to account for this.
3. The Committee stated that re-identifiable health research data must be stored for individual participants 10 years following them turning 16, not a blanket 10 years from study start. (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019,* para 6.28*)*
4. The Committee stated it was unclear if any data would be sent overseas. Please clarify. *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019,* Chapter 12*).*
5. The Committee asked for clarification if the younger participants had modified questionnaires for simplicity, as well as tailoring interviews for being age-appropriate (e.g., not asking children about finances) and having the option to have the participating parent present for younger children. Please also make it clear in the relevant participant information/assent forms that this is what participation involves. *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019,* para 6.22d*).*
6. The Committee noted that the study was not collecting ethnicity data. Researchers must collect ethnicity data unless there is a valid justification for why this is not necessary. (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019,* para 9.10 & 9.20*)*
7. The Committee queried how participants will be recruited. The researcher responded that parents who have consented to being contacted for future research from a database will be contacted for participation. The Committee noted that the letter should be reworded to refer to the fact that that they have previously consented for this contact; and the invitation to children aged under 16 is included in the letter to parents.

The Committee requested the following changes to the Participant Information Sheet (PIS) and Consent Form (CF) *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019,* paras 6.22d & 7.15 – 7.17):

1. The Committee noted there are missing sections of the participant information sheet in order to obtain fully informed consent. The Committee recommended the Researcher adapt the [PIS template available on the HDEC website.](https://ethics.health.govt.nz/guides-templates-and-forms/participant-information-sheet-templates/) This can be used as a guide.
2. Assent forms are missing information sheets. Please ensure age-appropriate information is provided. Additionally, a parental consent form is required along with assent.
3. Please be clear that this is a pilot study and what this pilot is for.
4. Please clarify to both parents and children that parents will be responding to questions about their views on both themselves and the child.
5. Additionally, make it clear to children consenting for themselves that their parents will be providing information about them too.
6. Please consider the potential that the parent who has experienced the TBI will be aware of the study and that it may be potentially distressing and how this might be managed with participants and the non-participant parent.

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 researchers to resubmit to Northern A.

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| **3** | **Ethics ref:** | **21/NTA/152** |
|  | Title: | ITL-2002-CL-001 (Resubmission): A Study to Evaluate NTLA-2002 in Patients with Hereditary Angioedema (HAE) |
|  | Principal Investigator: | Dr. Hilary Longhurst |
|  | Sponsor: | Simbec-Orion |
|  | Date submitted: | 05 August 2021 |
|  | Clock Start Date: | 05 August 2021 |

Dr Hilary Longhurst, Shuruthi Balachandran, Courtney Rowse, Professor Edward Gane, Michael Maitland and Jim Butler 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. NTLA-2002 is an investigational drug being developed as a potential new treatment for patients with Hereditary Angioedema (HAE). HAE is a rare, genetic disorder that is characterised by severe recurring and unpredictable inflammatory attacks in various organs and tissues of the body which can be painful, debilitating, and life-threatening. NTLA-2002 consists of a CRISPR/Cas9 gene editing system, which is able to disable the abnormal gene that is responsible for HAE. This CRISPR/Cas9 gene editing system has been used in a small number of patients in a previous study (20/NTA/129) for Transthyretin Familial Amyloid Polyneuropathy. This first-in-human (FIH) study will aim to assess the safety and tolerability of NTLA-2002 in patients with HAE. The study is comprised of 2 phases, referred to as Part 1 and Part 2 (approx. 30 patients in Part 1 and approx. 25 patients in Part 2). Part 1 will evaluate different dose levels of NTLA-2002 and assess how the body responds. If Part 1 identifies a safe and effective dose (defined by blood results and an observed reduction in HAE attacks) then the study will proceed to Part 2. The doses selected for Part 2 will be determined to be safe, effective and well tolerated based on the information from Part 1. Patients will be enrolled in the study for approximately 2 years, in which there will be a screening and treatment period, followed by a long-term follow up period. Depending on which part of the study and what group they are enrolled in, they will either receive a single dose of NTLA-2002 or placebo (if randomised to placebo arm in Part 2). The results from this study will be used to inform further clinical development of NTLA-2002.

Summary of resolved ethical issues

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

1. The Committee acknowledged the significant changes made from the last submission.
2. The Committee confirmed with the researcher that sentinel dosing is occurring.
3. The Committee noted the low risk of cytokine storm and queried whether the site will be equipped to manage this if this occurred in a participant. The researcher confirmed that this is the case, and a management plan is in place.

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 about the novelty of CRISPR/Cas9 in New Zealand noting that it is not covered well under New Zealand regulation. As noted on the initial application, approval from the Gene Therapy Advisory Committee (GTAC) is required before ethics committee approval can be given. The Committee was provided with some correspondence between the researcher and GTAC and found the questions raised by GTAC consistent with their concerns. One of the outstanding concerns is the status of the CRISPR/Cas9 gene editing in vivo and whether that requires EPA approval. The Committee noted that obtaining EPA approval, if required, is also part of the GTAC approval process. The Committee queried if the researcher could confirm what discussions happened around this. The researcher responded that EPA approval discussion did not occur with GTAC and that they have addressed all issues raised by GTAC. The researchers noted that with a previous similar study, there were discussions with EPA, which had advised them that a formal EPA submission was not required. The Committee requested that the researcher provide evidence of whether EPA approval is or is not required for this study.
2. Revised documentation in the Protocol discusses likely long-term follow up but there is no detail in the participant information sheet (PIS) that informs participants that their responsibilities potentially go beyond the end of the study and what this might involve. It was agreed that information about this should be added to the current PIS as its own section, rather than as a separate amendment.
3. The Committee queried how and by whom the long-term follow up would be managed and what it would entail. The researcher responded that the follow up would be sponsor-driven. The Sponsor noted that there is no standard method for managing long-term follow up and would compile guidance internationally before submitting the follow-up plan protocol as an amendment. The Committee requested that this is submitted within the next 12 months.
4. The Committee stated that the Part 2 PIS cannot be approved as part of this application as Part 1 informs the dosing for Part 2 and should be submitted as an amendment when it is required.

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

1. Please include a section about the long-term follow up for this study, noting that further information will be provided once it becomes available. Please include discussion of ‘off-target’.
2. The cover letter notes that some participants may not be able to view the video themselves, and that they can do so with the study doctor. Please add this to the PIS.
3. The Committee requested the researcher include more detailed contraceptive advice, utilising the wording in the [HDEC reproductive risks template.](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-reproductive-risks-apr20.docx)
4. Please add full Laboratory details to all PISs.
5. Please note that reimbursement payments can be flexible, such as if a participant requires time off and needs more immediate compensation to avoid undue burden.
6. Please specify the specific time points for blood sample collection (e.g., how often in a day) and indicate the amount of blood per extraction.
7. Please specify whether the blood extraction procedure is through direct IV or venous cannula.

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 feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement,* paras 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 Sotera Catapang.

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| **4** | **Ethics ref:** | **21/NTA/131** |
|  | Title: | SNAP |
|  | Principal Investigator: | Dr Genevieve Walls |
|  | Sponsor: |  |
|  | Date submitted: | 22 July 2021 |
|  | Clock Start Date: | 05 August 2021 |

Dr Genevieve Walls, Dr Rachel Webb, Dr Steven Tong, Nicola Jackson and Jocelyn Mora 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. SNAP aims to identify the effect of a range of clinical interventions on all-cause 90-day mortality in patients with staphylococcus aureus bacteraemia (SAB). SNAP is an international investigator-initiated, Randomised Embedded Multifactorial Adaptive Platform trial aiming to enroll 6000 patients worldwide over 4 years. It includes three domains: Antibiotic Backbone, Adjunctive Treatment, and early oral switch. The adaptive design allows multiple questions to be evaluated simultaneously and sequentially, evaluating interactions between different treatment options, to determine the optimal combination of treatments as rapidly as possible.
2. SNAP also involves storage of bacterial isolates to form biobanks and creation of a SAB registry for future research in New Zealand and worldwide and the optional consent for data linkage to existing datasets (e.g. Ministry of Health) will also be sought. Patients can consent to the registry without consenting to the study.

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 researchers will be using identifiable information without consent to screen for potential participants to this study. The Committee granted a waiver of consent on the grounds of scientific validity.
2. The Committee noted that storing bacteria does not count as a biobank according to the HDEC SOPs. Therefore, no governance documentation is required for bacteria being stored at Middlemore Hospital. Participants do need to be informed of where their bacteria is being stored and what it is being used for, and it is useful to note that no human tissue will be stored.
3. The Committee noted that if participants would like to withdraw from the study, it is not legally necessary for them to fill out of a withdrawal form. The researcher agreed they would not require participants to fill out a withdrawl form, and would allow participants to specify which parts of the study them would like to withdraw from and which they might like to remain in.
4. The Committee noted the complexity of the assent forms but decided that they were age appropriate.

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 in New Zealand, people cannot consent on behalf of non-consenting participants and there is no surrogate consent. Rather, medical practitioners can enrol non-consenting participants under a best interests justification (*Code of Health and Disability Services Consumers' Rights,* right 7(4)) and must seek the views of people with an interest in the participant when doing so. The enrolment of nonconsenting participants was not approved for this study.
2. The Committee advised the researchers to submit the following documents as an amendment to the study, for full committee review, if they wish to proceed with the enrolment of nonconsenting participants:
   * An amended protocol and PISCFs, reflecting the process, conditions, and justifications for enrolling a participant under a best interests justification.
   * Consider including a table attached to the RSA that outlines the various consenting scenarios, e.g. if a participant is unconscious or too unwell to consent, if a participant regains the ability to consent after the study has begun (consent to continue in the study), and the process for those patients who pass away in hospital.
   * PISCFs reflecting the scenarios above e.g. an information sheet for seeking the views of people interested in the participant’s welfare, with a place for a signature

The Committee noted that it would be difficult to prove a best interest justification for enrolling nonconsenting participants to the data registry, and they may wish to seek further advice on this from other platform adaptive trial investigators.

1. The Committee noted that the Data Management Plan needs to have more detail on what data will be linked and how often this will be done.

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

MAIN PIS

1. Please inform the participant that it is bacteria rather than their tissue that is being stored.
2. Please clarify who the sponsor is.
3. Please inform the participant of their rights of withdrawal from this study.

REGISTRY PIS

1. Please inform the participant why they are being approached to be part of the data registry (e.g. they were screened and not eligible for the study or they chose not to participate in the study).
2. Please inform the participant what data will be linked, from which databases and registries, and for how long this follow-up will occur.
3. Please clarify who the sponsor is.
4. Please inform the participant of their rights of withdrawal from this study.

Decision

This application was *provisionally approved* by consensus, for prospectively consented patients, 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*, 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 Michael Meyer and Mrs Helen Walker.

Please submit an amendment for full committee review, detailing the best interests justification, in order to proceed with enrolment of nonconsenting participants to this study.

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| **5** | **Ethics ref:** | **21/NTA/130** |
|  | Title: | Comparison of two rosuvastation formulations. |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Aspen Australia |
|  | Date submitted: | 22 July 2021 |
|  | Clock Start Date: | 05 August 2021 |

**CLOSED MEETING.**

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| **6** | **Ethics ref:** | **21/NTA/135** |
|  | Title: | 177Lu-DOTA-TLX591-CHO safety, biodistribution and dosimetry study (PROSTACT-Select) |
|  | Principal Investigator: | Dr Remy Lim |
|  | Sponsor: | Telix Pharmaceuticals (NZ) Ltd |
|  | Date submitted: | 23 July 2021 |
|  | Clock Start Date: | 05 August 2021 |

Dr Remy Lim 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. Patients with metastatic castration-resistant prostate cancer (mCRPC) have a less than 1/6 chance of surviving 5 years and need new treatment options. Prostate specific membrane antigen (PSMA) is a protein expressed in abundance by mCRPC cells. Telix is developing a radioligand therapy combines a targeting compound (antibody TLX591) that binds to PSMA in mCRPC cells, and a radioactive isotope (177Lu), causing DNA damage that inhibits tumour growth and replication. This therapeutic approach enables targeted delivery of radiation to the tumour, while limiting damage to the surrounding healthy tissue. This is Phase I study to confirm the safety, tolerability, biodistribution and dosimetry of the 177Lu-TLX591-CHO. Up to 50 eligible patients will receive two single intravenous injections of the study drug plus best standard of care. There could be the benefit that the prostate cancer will respond very well to the additional treatment, providing a new treatment option for mCRPC.

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 application stated that future unspecified use of tissue will be undertaken. The researcher clarified that this is not the case – there will be no future unspecified use of tissue.
2. The Committee noted that the researcher’s answer to question r1.7.1.2 of the application form states that the study will not be carried out principally for the benefit of the manufacturer. The Committee clarified that the study *will* be carried out principally for the benefit of the manufacturer and the researcher agreed.
3. The Committee noted that advertising / recruitment material can be used but must not take the place of the PIS.

Summary of outstanding ethical issues

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

1. The Committee requested that the researcher check with the sponsor that related data usage in this study and for future unspecified research (FUR) is truly optional.
2. The Committee requested that the researcher provides NZ specific insurance.
3. The Committee noted that the Data and Tissue Management Plan (DTMP) included in the protocol did not meet all of the relevant standards set out in chapters 12-14 of the *National Ethical Standards for Health and Disability Research and Quality Improvement*, 2019. Please update the DTMP to meet all relevant standards. Please refer to the [HDEC DTMP template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/hdec-data-tissue-management-template-oct2020.docx) on the HDEC website for guidance.
4. The Committee noted that the study protocol states that if a participant cannot provide consent, a legal representative can do so on the participant’s behalf. This is not legal in NZ. Please remove this statement from the protocol (or make clear that this provision does not apply in New Zealand).
5. Please provide a Data Safety Management Board Charter.
6. Please provide copies of the surveys, referred to on page 7 of the PIS.
7. The Committee noted that the CI indemnity has expired. Please provide an updated indemnity certificate.
8. The Committee noted that the biodistribution phase of the study is not a sub-study. Please update the study protocol to make this clear.
9. The Committee noted that the study documentation states that tissue samples will be sent overseas with identifiable information (participant date of birth and initials). The Committee stated that only de-identified information (study code) can be sent with the samples.
10. The Committee requested that identifiable information is not collected with the study surveys. Rather, please use a study code.
11. Please ensure that no patient identifiers are included with images sent overseas.

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

1. Please provide a lay title on page 1 of the PIS.
2. Please clearly disclose on page 1 of the PIS that this is a first in human trial. Later in the PIS you can explain that similar studies have been done.
3. Please proofread the PISCF for typos. E.g., on page 4, it should say ‘visit 5’.
4. On page 10, please remove the duplicated phrase “the dose from this study is comparable to that received from several CT scans”.
5. If related data usage in this study and/or for FUR is truly optional, please give this its own PISCF so that it is made clear to participants that it is optional.
6. Please make it clear on page 5 that the first 5 participants enrolled in the study will be involved in the biodistribution phase of the study. Provide more information regarding the additional procedures and risks (i.e. related to the SPECT scan).
7. Please list the sponsor in the ‘who pays for the study’ section.
8. Please update the wording on contraception. Please refer to the standard wording in the [HDEC reproductive risks template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-reproductive-risks-apr20.docx) for guidance.
9. Please provide more information on what will happen to tissue – e.g. where it will go, how it will be disposed of, what happens to it when a patient withdraws from a study. Please include a Māori tissue statement. Please see the [HDEC PISCF template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc) for guidance.
10. Please clarify the wording in the risks and benefits section.
11. Please quantify the risk of contracting fatal cancer in the future, in lay friendly terms.
12. Please make consistent across the PISCF whether or not it is optional for a participant to withdraw data that has already been collected.
13. Please include in the main body of the PIS that blood will be sent overseas, including the address of where it will be sent, what will happen to it and how it will be disposed of.
14. Please seek consent to inform the participant’s GP that they are taking part in the study. Include this information in the PIS.
15. Please upload standard site information sheets regarding nuclear medicine.

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*, 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 Kate Parker and Mr Dominic Fitchett.

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| **7** | **Ethics ref:** | **21/NTA/136** |
|  | Title: | DoxAPrem Study |
|  | Principal Investigator: | Dr Christopher McKinlay |
|  | Sponsor: | The University of Auckland |
|  | Date submitted: | 23 July 2021 |
|  | Clock Start Date: | 05 August 2021 |

Dr Christopher McKinlay 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.

Michael Meyer declared a potential conflict of interest as he is a co-investigator for this study. The Committee decided that he would leave the meeting for discussion of this application.

Summary of Study

1. The aim of this study is to evaluate use of doxapram by the oral route for treatment of apnoea in very preterm infants (pauses in breathing with desaturation and/or bradycardia). Apnoea occurs in approximately 70% of infants born at 32 weeks' gestation and is associated with delayed feeding, increased mortality and increased risk of neurodevelopmental impairment and long-term respiratory morbidity. First line treatment of apnoea involves continuous positive airway pressure (CPAP) and caffeine treatment. Infants who are refractory to caffeine are usually trialled on doxapram, an alternative respiratory stimulant. Traditionally doxapram has been given by continuous intravenous infusion, but long-term intravenous access can be difficult to maintain and increases the risk of sepsis. Several studies have found that oral doxapram is equally effective but the optimal oral dose in preterm infants is unclear. This trial will compare two oral doses of doxapram (12 mg/kg vs. 24 mg/kg 6 hourly) to determine which is more likely to achieve therapeutic blood concentrations. Plasma concentrations will also be used to develop a pharmacokinetic model to optimise dosing based on gestation and postnatal age. Effect of oral doxapram on respiratory parameters and tolerance will also be assessed.

Summary of outstanding ethical issues

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

1. The Committee requested that the researcher refers to the HDEC [data and tissue management plan template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/hdec-data-tissue-management-template-oct2020.docx) on the HDEC website for guidance about relevant sections that may be missing from their protocol.
2. Please provide a signed peer review.
3. Please include a table of procedures in the protocol, detailing associated risks.
4. Please upload documentation of CI indemnity and site insurance.
5. Please clarify whether this is a feasibility study, and if so what feasibility objectives are being sought

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

1. Please replace the term ‘caregiver’ with ‘legal guardian’.
2. Please discuss data and tissue management in the PIS. Please refer to the [HDEC PIS template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc) on the HDEC website for guidance.
3. Please include a table of procedures, in lay language. Include information on the associated risks.
4. Please update the advocacy email address.
5. Please include a subheading for data collection so that it is clear for participants that data includes pregnancy and data collection about the child.
6. Please clarify that babies will already be on caffeine (as an inclusion criteria).
7. Please clarify that the blood tests are just for the levels of the drug and not for anything else.

Decision

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

* please address all outstanding ethical issues raised by the Committee
* please update the Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee.

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| **8** | **Ethics ref:** | **21/NTA/138** |
|  | Title: | Short-term exposure to biodiversity and health |
|  | Principal Investigator: | Dr Collin Brooks |
|  | Sponsor: | Massey University |
|  | Date submitted: | 30 July 2021 |
|  | Clock Start Date: |  |

Dr Collin Brooks and Jeroen Douwes 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.

Karen declared a potential conflict of interest as she is working with Jeroen Douwes on a different study. The Committee decided that it was not a conflict of interest as Karen is not involved in this particular study.

Summary of Study

1. The study aims to determine if short-term exposure to an environment rich and diverse with plants changes gut bacteria, immune markers and asthma and allergy symptoms. Specifically, it will use a randomised crossover design to assess the effects of biodiverse exposure on asthma, allergy, airway inflammation, commensal microbiota, and serum immune markers in fifty to sixty (60 will be recruited) asthmatic schoolchildren (11-16 yrs).
2. Participants will be assessed at baseline for respiratory symptoms, lung function, airway inflammation (fractional exhaled nitric oxide (FENO)), atopy (this will only be done at first visit, if not done previously as part of HRC15/311), wellbeing and nature connectedness, and a stool and blood sample will be collected.
3. They will then be randomly assigned to two groups of the same size, with one asked to visit a high vegetation diverse area at least twice, and for a minimum of 2 hours a week, for a 3-month period.
4. The other group will conduct themselves as normal, but whenever possible, avoid the pre-identified area of high biodiversity for the same 3-month period. Within this period, local soil and air samples (representative of each exposure for each child) will be collected for 16s microbiome sequencing.
5. At the end of the 3-month period, all participants will repeat the assessment described above. Participants will then be asked to return to normal behaviour (with associated exposures) for the following nine-month period (“washout”). At the same time the following year (to control for environmental variation/pollen exposure), participants will be asked to “crossover”, and undergo the corresponding exposure (i.e. children previously asked to visit biodiverse areas would now be requested to avoid them and vice versa).
6. Local soil and air samples will again be collected for 16s microbiome sequencing. At the end of this second exposure period, all participants will repeat the full assessment described above.

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 researchers do not have consent to use identifiable health information to contact past study participants to invite them into this study. The Committee granted a waiver of consent for this access of data, with the exception of instances where past participants had indicated that they no longer wanted to be involved in the previous study, or that they did not want to be contacted, or where the researchers had stated that they would not be retaining the participant’s details.
2. The invitation letter for this study was approved.
3. The researchers noted that they are satisfied with the insurance cover they have from the university.

Summary of outstanding ethical issues

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

1. Please provide the form for recording peak flows.
2. The Committee did not approve consenting participants for future unspecified research. If the researcher later decides they would like to do this, this will need to be submitted as a study amendment.
3. Please update the protocol to specify that the study will be paying for the participants’ Zealandia passes and please clarify the monetary value of these passes.
4. The Committee noted that 16-year-old participants should be provided the opportunity to provide their own consent, rather than assent.
5. The Committee noted that the children’s study data must be kept for 10 years after the oldest participant turns 16. Please clarify this in your study documentation.
6. The Committee noted that the researchers are keeping the samples for 10 years for study related purposes, currently unable to be specified. This requires extended consent. Please make this clear in the protocol.
7. The Committee noted the high rates of asthma amongst Māori and requested that the researcher updates the study protocol to include a plan for proactively recruiting Māori participants into this study.

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

1. Please inform the participant that you will be using data collected from the previous study, and seek consent to do so.
2. Please clarify what is required of participants in this study, e.g., recording their peak flows.
3. Please inform the participant that Zealandia will be recording the participants' visit history.
4. Please provide more detail around which samples will be sent overseas, where specifically they will be sent, and what will happen to them.
5. Please provide age-appropriate information sheets for children.
6. Please modify the assent forms to match what is in the information sheets.
7. Please specify that contacting the GP will include low mood indicated through the questionnaires and / or professional judgment of the study nurses.
8. Please move information about what blood tests you will be doing into the blood sample section.
9. Please clarify in the PISCF that you are seeking extended consent for future study-specific use of tissue.
10. Please update the ACC compensation statement. Please refer to the [HDEC PISCF template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc) on the HDEC website for guidance.
11. Please include information about participant rights to access or correct their data and how the data will be stored.

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*, paras 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 Michael Meyer.

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| **9** | **Ethics ref:** | **21/NTA/142** |
|  | Title: | Genetic markers in ovarian cancers in New Zealand (NOVel) |
|  | Principal Investigator: | Doctor Bryony Simcock |
|  | Sponsor: |  |
|  | Date submitted: | 02 August 2021 |
|  | Clock Start Date: | 05 August 2021 |

Dr Bryony Simcock 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. This project will establish a national programme for New Zealand women diagnosed with epithelial ovarian cancer. This will enable women to participate in local and international research studies. This will involve collecting clinical information about the diagnosis, treatment and ongoing management for women with epithelial ovarian cancer. All consented women will have a sample of tissue and blood stored at the time of the initial diagnosis and at any recurrence of the disease as part of routine clinical care. This tissue will be stored in the local tissue bank laboratory. At some stage in the future tissue samples will be tested for specific markers to create its own unique profile. It is this profile that enables researchers to then select appropriate trials for women to be invited to participate in. Many women with ovarian cancer require a biopsy for clinical purposes. Little is known about the experience for women. Women will be asked to complete a short questionnaire on the impact of having a biopsy.

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 although the researcher only has funding secured for the first 20 participants, this study is not a pilot.
2. The researcher clarified that there will be separate study specific consent and tissue bank consent.
3. The researcher clarified that the questionnaires had been taken from a pre-established program but simplified for this study.
4. The Committee clarified with the researcher that biopsies will only be taken for diagnostic purposes.
5. The Committee queried whether post-biopsy questionnaire section on feelings will be affected by whether or not the patient has their biopsy results. The researcher responded that most patients already are aware of the severity of their diagnosis pre-biopsy.

Summary of outstanding ethical issues

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

1. The Committee requested that the researcher localise the study documentation for a NZ context.
2. Please provide information in the Protocol, and clarify for participants in the PISCF, what the relationship of the NZ study is to Inovate in Australia. Please clarify when tissue is sent to Westmead in Australia, what (if any) participant data is also provided.
3. Please provide a data management plan, with particular attention to who will be seeing what data and in what form (identifiable vs. de-identified) (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019,* chapter 12).
4. Please clarify in the protocol that no participant information will be shared with sponsors of trials without consent.
5. Please provide more detail in the protocol surrounding the process for actionable results and incidental findings, and how these will be communicated to the participant. (*National Ethical Standards for Health and Disability Research and Quality Improvement*, paras 14.23-14.26)
6. Please clarify in your protocol which samples are study specific and what is for the tissue bank, the relationships between the tissue banks, and how this will be consented for.
7. Please clarify whether you will have governance over samples in the tissue bank or whether they will join the general pool, accessible to other researchers.
8. Please provide further information in the protocol, and a plan for informing and consenting participants around generating cell lines, in a separate PISCF.
9. Please explain further what the purpose of the serial blood testing is for.
10. Please provide further information about data linking, for example whether it is just once or ongoing. Please clarify in the protocol / DMP and the PISCF.

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

1. Please explain how data will be managed.
2. Please explain in the PIS that one of the purposes of this study is to be able to have NZ women partake in international trials and how sharing of participant profiles to determine eligibility for international trials will work. Please provide a consent clause for this in the CF.
3. Please explain in lay language in the PIS what the serial blood tests will be testing for (e.g. is this for circulating tumour DNA?)
4. Please include a consent clause in the CF confirming consent for genomic testing and sequencing.
5. Please upload the tissue bank consent forms.
6. Clarify in the PIS that the tissue will be mostly used in this study, and excess tissue will be kept in the tissue bank.
7. Please provide a PISCF tailored specifically to what you are trying to do around the cell lines, including whether this is optional (*National Ethical Standards for Health and Disability Research and Quality Improvement*, para 16.5).
8. Please clarify how many biopsies the participant will be subject to.
9. Clarify whether the Cancer Society is a funder of the study, and if so include this in the PISCF.
10. Clarify that women with new diagnosis of ovarian cancer, peritoneal or fallopian cancer, or recurrent ovarian cancer, may participate in the PISCF (if this is the case, as indicated in the study documentation).

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 their application to NTA, for the sake of continuity.

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| **10** | **Ethics ref:** | **21/NTA/154** |
|  | Title: | (duplicate) HRcSCC |
|  | Principal Investigator: | Mr Richard Martin |
|  | Sponsor: |  |
|  | Date submitted: | 04 August 2021 |
|  | Clock Start Date: | 05 August 2021 |

Mr Richard Martin and Dr Teresa Holm 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. All patients diagnosed with high-risk cutaneous squamous cell carcinoma and had a sample of this tissue taken at Waitematā DHB between 11 January 2007 and 30 June 2021 will be offered the opportunity to participate in a research study. The study wants to learn more about why and how these cancers are sometimes easily treated without further complication and some behave more aggressively spreading throughout the body. The research study will examine tissue samples to identify any genetic differences between the tissues of those whose cancer spread compared with those whose cancer did not spread. This information may be useful to better understand the biology of this disease and in turn build knowledge on how best to treat future patients.
2. This study will examine high-risk cutaneous Squamous Cell Carcinomas that have spread to lymph nodes compared to those that did not spread. Tissue will be sourced from archival formalin-fixed, paraffin-embedded tissues taken and stored at time of initial excision at WDHB General Surgery skin service. The tissue will be sent to the USA to undergo molecular testing. In order to carry out these tests the tissue will be destroyed in the process and therefore cannot be returned to New Zealand. Secondary outcomes of the study that will be recorded are disease-free survival, time to recurrence and overall survival.

Summary of resolved ethical issues

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

1. The researcher clarified that tissue of deceased participants will not be used if enough living participants consent to being enrolled in the study.
2. The Committee noted that eligible participants are identified by a database and queried whether they know that they are on this database. The researcher responded that they are aware, and enrolments to the database in the last six years entailed consent.
3. The Committee queried whether tissue blocks should be sent to the USA only in instances where there is excess tissue, allowing tissue to remain in NZ to be available for future use. The researchers responded that they could not anticipate a need for that tissue in the future, as any future analysis would require a fresh tissue sample to be taken.
4. The researcher clarified that the research is being paid for through a research fund.
5. The Committee queried the potential for incidental findings when doing genomic analysis. The researcher responded that this is a possibility, but that it will be epigenetic information relevant to the tumour. Any incidental findings in the genomic analysis of the tumour will not be fed back to the participant, as it will be assumed to be because it is abnormal DNA that is not necessarily in their germline. There will be no germline sequencing.
6. The Committee queried if identifiable participant information will be sent overseas. The researcher responded that all patient data accompanying the tissue will be de-identified, only including age and gender.
7. The Committee queried whether it is possible for the tissue analysis to be done in NZ. The researcher responded that it is very difficult to successfully do RNA sequencing from tissue blocks in NZ.

Summary of outstanding ethical issues

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

1. The Committee noted that the researcher did not have a protocol in place for approaching the relatives of deceased participants. The Committee decided to approve the study for living participants and informed the researcher that they can submit an amendment to use the tissue of the deceased without consent if the need arises. On this basis, the PISCF for relatives of the deceased was not approved. If developing an amendment for deceased patients relatives, please revise as the current format/wording is likely to cause distress. Please also consult with patient groups regarding the use of deceased tissue.
2. The Committee requested that the researcher undertake Māori consultation.
3. The Committee requested that the researcher look at section 14 of the *National Ethical Standards for Health Research and Quality Improvement*, 2019 and ensure that the protocol and PIS meets these standards for handling genetic information.
4. The Committee noted that ethnicity data must be collected. Please update the study protocol to reflect this.

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

1. Please inform the participant in the participant information sheet that their GP will be informed, or remove this from the consent form.
2. Please remove tick boxes on the consent form unless these are truly optional consent clauses.
3. Please include information about patient rights to withdraw from the study. Please see the current [HDEC PISCF template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc) on the HDEC website for guidance.
4. Please include a cultural tissue statement in the PIS. Please refer to the [HDEC data tissue management plan template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/hdec-data-tissue-management-template-oct2020.docx) for guidance.

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*, paras 7.15 – 7.17).

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

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| **11** | **Ethics ref:** | **21/NTA/132** |
|  | Title: | 272HV111: A Study to Evaluate Diroximel Fumarate (BIIB098) in Healthy Chinese and Caucasian Adults |
|  | Principal Investigator: | Dr. Chris Wynne |
|  | Sponsor: | IQVIA |
|  | Date submitted: | 22 July 2021 |
|  | Clock Start Date: | 05 August 2021 |

Dr Chris Wynne 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. Diroximel Fumarate (DRF; BIIB098) was developed for the treatment of relapsing forms of Multiple Sclerosis (RMS) and was approved by the US FDA in 2019, and is sold under the trade name VUMERITY®. As of July 2020, an estimated 1461 participants had received DRF across a number of studies, in which DRF was demonstrated to be safe and well tolerated when administered at dosages between 49 mg - 980 mg.
2. Multiple Sclerosis (MS) is a chronic inflammatory disease in which the body’s immune system attacks the protective covering of the nerves. This results in nerve damage and disrupts the communication between the brain and the body. MS can cause many different symptoms, including vision loss, pain, fatigue, and impaired coordination. Although the pathophysiology found in MS is considered to be similar in Caucasian and Asian populations, there is still insufficient pharmacokinetic (PK) data of DRF in the Chinese population. The aim of this study is to compare the levels of DRF in the blood (PK) between healthy Caucasian participants and healthy Chinese participants.
3. Approximately 32 healthy participants will take part in this study at both NZCR and a site in Hong Kong. The study will be comprised of 2 groups, with each group consisting of 16 Chinese participants and 16 Caucasian participants. The Chinese population will be recruited and enrolled at the site in Hong Kong, and NZCR will enrol the Caucasian participants. All participants will receive DRF 462 mg twice daily, for 4 consecutive days, and once on the fifth day. This will be administered orally in the form of a tablet.
4. Blood samples to measure the body's response to DRF will be collected at specific time points during the study, safety will be closely monitored, and any changes in health recorded.

Summary of resolved ethical issues

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

1. The Committee clarified with the researcher that this is not a first in human trial.
2. The Committee queried the justification for excluding other ethnic groups other than Caucasian from participating in this study. The researcher responded that as the metabolism of this medication is impacted by ethnicity, the homogeneity of the comparator group was important for comparing against the Chinese participant group.
3. The Committee queried whether five doses is necessary, and the researcher responded that it is to gain a better understanding of how the drug accumulates.
4. The Committee asked when participant follow up occurs. The researcher responded that this would occur on day 10.

Summary of outstanding ethical issues

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

1. Please ensure that the insurance policy for this study is NZ specific.
2. The Committee queried why samples were being retained for 25 years. The researcher responded that this is sponsor requirement. Please follow up with the sponsor to request that samples are stored for 15 rather than 25 years.

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

1. Please inform the participant that Covid is a notifiable disease.

Decision

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

* please address all outstanding ethical issues raised by the Committee
* please update the Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee.

## Substantial amendments

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| **1** | **Ethics ref:** | **20/NTA/75/AM06** |
|  | Title: | GPX Embolic Device Study |
|  | Principal Investigator: | Associate Professor Andrew Holden |
|  | Sponsor: | Ms Libble Ginster |
|  | Date submitted: | 05 August 2021 |
|  | Clock Start Date: | 03 August 2021 |

Associate Professor Andrew Holden, Helen Knight and Elleni Takele were present via videoconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. Catheter embolization involves occluding, or blocking, a blood vessel to stop blood supply to a specific area. This type of procedure is usually performed to control or prevent abnormal bleeding and is an alternative to open surgery.
2. This First in Human study is intended to provide essential clinical information as to the safety profile of the GPX Embolic device and build on previously captured pre-clinical data.
3. It is anticipated the GPX Embolic device will provide more precise control of the embolic material delivery to the target location compared to currently marketed embolic materials while providing equal or potentially superior occlusion of the target vessel.
4. This amendment seeks to restart the study after the study was placed on hold as the result of the death of a participant.

Summary of resolved ethical issues

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

1. The researcher noted that participants who have exited the study will not be reconsented.

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 received an update from the Secretariat on a separate complaint process underway involving this study, and confirmation of the HDEC’s role in terms of reviewing this amendment. The Committee noted that, arising from the complaint, there is an independent audit of the consent process at the study locality (not study specific) which is not yet complete. HDEC approval of this study to recommence is provisional on the results of that audit.
2. The Committee requested that the researcher clarify in the protocol when the low viscosity and high viscosity agents will be used.
3. The Committee requested that the researcher update the protocol to include information about the independent safety committee, such as who they are and how often they meet.
4. The Committee noted that legally authorised representatives are not allowed to provide consent in NZ for a study of this nature. Please remove this from the study protocol.
5. Please check that there is no further report yet to be received from the independent safety (Adverse Event) committee. If there is an outstanding report, please provide this for HDEC review.

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

1. Page 2 of the PIS is too vague about why the study was paused. Please include information about the adverse events, noting that the protocol has been changed as a result. Ensure that this explanation is described in lay-friendly terms.
2. The participants must be adequately informed of the risks of enrolling in this study. It is misleading to say that this study has a 0.5-5% risk. Please provide data from the safety report, noting that there were nine SAEs involving five participants out of 10, and there were five AEs. In the table, please provide percentages of participants that have suffered each adverse event. As discussed, separating the cases into the groups for which the new inclusion/exclusion criteria applies will be helpful in further explanation.
3. On page 5, please remove the statement saying that “initial use during this study have shown a good safety profile in patients”. Please state death as a risk of participation.
4. Please provide more context for the risk of migration of the embolic agent.
5. Please remove the statement about tissue samples being sent overseas, as this is not occurring.
6. Please provide more information about the remote presence of sponsor during the study procedure, with particular regard for data confidentiality and identifiability. Please refer to the [HDEC PISCF template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc) on the HDEC website for guidance.

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*, paras 7.15 – 7.17).

After receipt of the information requested by the Committee, a final decision on the application will be made by the full committee.

## Review of approved studies

## General business

1. The Committee noted the content of the “noting section” of the agenda.
2. The Chair reminded the Committee of the date and time of its next scheduled meeting, namely:

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| **Meeting date:** | 21 September 2021 |
| **Meeting venue:** | TBD |

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 7.45pm.