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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 15 June 2021 |
| **Meeting venue:** | ONLINE - Zoom Meeting |

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| **Time** | **Item of business** |
| 1.00pm | Welcome |
|  | Confirmation of minutes of meeting of 18 May 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 | 21/NTA/95 Sotera / Catherine  21/NTA/91 Sotera / Catherine  21/NTA/93 Kate P / Rochelle  21/NTA/94 Karen / Rochelle  Break  21/NTA/83 Karen / Kate O  21/NTA/96 Kate P / Kate O  21/NTA/101 Karen / Kate O  21/NTA/102 Sotera / Catherine |
| 5.00pm | 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 | 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 | Present |
| Ms Catherine Garvey | Lay (the law) | 19/03/2019 | 19/03/2022 | Present |
| Dr Sotera Catapang | Non-lay (observational studies) | 11/02/2020 | 11/02/2023 | Present |
| Dr Michael Meyer | Non-lay (health/disability service provision) | 11/02/2020 | 11/02/2023 | Apologies |

## Welcome

The Chair opened the meeting at 1pm and welcomed Committee members, noting that apologies had been received from Dr Michael Meyer.

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 18 May 2021 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **21/NTA/95** |
|  | Title: | Non-Invasive Ventilation Mask Assessment |
|  | Principal Investigator: | Dr Robert Martynoga |
|  | Sponsor: | Fisher & Paykel Healthcare |
|  | Clock Start Date: | 03 June 2021 |

Jessica Fogarin 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.

Rochelle Style declared a potential conflict of interest on the basis that she is a potential beneficiary of a trust which owns some Fisher & Paykel shares. The Committee decided that she was able to participate in the discussion but not advocate for an approval if other members were more inclined to decline.

Summary of Study

1. An assessment of usability, perceived comfort and performance of the investigational Non-Invasive Ventilation (NIV) mask in the hospital environment. Eligible participants will use the study mask during their routine care and the Drs and Nurses assigned to the participants will be asked to complete a questionnaire on the usability, performance and perceived comfort of the mask. As the intended population can be vulnerable the investigation has been designed to have minimal disruption to the participants usual care.

Summary of resolved ethical issues

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

1. The researcher clarified with the Committee that some participants may have capacity to consent, and that there is a process to allow for this. However, many participants will not have the capacity to consent. These participants are not unconscious, rather they are not competent to consent due to respiratory failure and the need to be sedated.
2. The Committee queried whether the number of participants needed for the study could be recruited using only participants with the capacity to consent. The researcher responded that the site did not think this would be feasible.
3. The Committee noted that the researcher is claiming a best interest standard given that there is no option in NZ for a proxy consent by relatives. The Committee noted their concern that there is no clear articulation of best interest in the study documentation. The Committee queried whether data from a past study could be used as evidence that the mask is beneficial. The researcher clarified that this past study showed an over 80% preference for a very similar mask to the study mask. The mask in this study is of a similar fit to the past study mask but is designed to better enhance CO2 flushing. The fit of the mask in the previous study showed benefit in terms of increased comfort and decreased feelings of claustrophobia. This is still a relevant benefit for nonconsenting participants, who are sedated rather than unconscious. The Committee was satisfied that the best interest standard had been met but noted that this information needs to be included in the study documentation.
4. The Committee debated whether or not this is an observational or interventional study, with the researcher noting they had classified it as an intervention as a cautious approach. The Committee decided that it ultimately did not matter either way, as the best interest standard had been satisfied (subject to the researcher providing amended documentation supporting the explanation given orally to the committee).
5. The researcher clarified that the reason consenting participants are not completing the questionnaires is because many of them have never used a standard of care mask to compare the study mask against. Rather, there will an option for nurses to input patient feedback into their questionnaires.

Summary of outstanding ethical issues

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

1. Researchers must conduct their research according to a suitably detailed protocol. Protocols must include all information that is relevant for the type of study. *National Ethical Standards for Health and Disability Research and Quality Improvement* para 9.7-9.8.
   * The Committee requested that the researcher updates the protocol to detail the best interest justification.
2. Participants must receive the information that a reasonable consumer, in that consumer’s circumstances would need to make an informed choice or give informed consent prior to their decision to participate in research. *National Ethical Standards for Health and Disability Research and Quality Improvement* para 7.15.
   * The Committee requested that the researcher update their documentation to not refer to opting in or out, rather to use the phrase “expression of views” and clarify that a clinician will do this in cases where a support person is not available for the participant.
   * Please remove “participant” from the questionnaires as this is confusing, seeing they will be filled out by the study nurse.
   * Please ensure opportunities for consent are provided in all likely scenarios, e.g. if a participant regains capacity consent. Please provide this documentation.
   * Please make the changes to the participant information sheets and consent forms requested below.

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

ALL

1. Clarify that the use of the smart trial platform which is hosted in Ireland complies with the new Privacy Act in the Health Information Privacy Code around data being stored overseas.
2. Please do not collect ethnicity data in the consent form.
3. Please include a picture of the mask.

WHANAU/PERSONS INTERESTED PISCF

1. Please reframe to explain and reflect the best interest standard, including amendments so that it is clear that persons interested are not consenting on behalf of participants. Rather, as per the protocol, persons interested are establishing that they understand the study and believe the participant would be interested in participating.
2. On page 1, please complete the sentence: “Some off their treatment settings will be.”
3. On page 2 please state that the hoped-for benefits may not be achieved – there’s no guarantee.
4. The following statement on page 2 must be amended: “What happens after the study if they do not want to participate? Patients who decide not to participate in the study will continue to receive NIV on the study mask because this treatment is the one most likely to benefit them. Their data and their Doctors or Nurses feedback will not be used in the study analysis in this situation.” If the patient does not wish to continue to participate, they must be allowed to have the standard of care mask and it can’t be stated that the study mask is the one most likely to benefit them.
5. Please provide more information in the data section on access and correction rights, coded data, storage etc. – please refer to the [HDEC template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc) for guidance.
6. Ensure there is an option for people to agree to continued use of the data already collected.
7. The CF should be completed for both scenarios – i.e., whether the person interested believes the patient would wish to participate in the research AND if they think the person would not wish to participate.

PARTICIPANT PISCF

1. Please do not use the term ‘caregiver’ to describe clinicians, as this is confusing.
2. Please include that there is the option to have the standard of care mask.
3. Please clarify that participants can withdraw their data.
4. Please amend the compensation section to withdraw the Medicines NZ statement as these guidelines do not apply for medical devices. Please ensure that the compensation wording is consistent with the guidelines that you are adhering to, if any, or otherwise describe the compensation terms.
5. Please add an area where the clinician clearly marks that they consider this to be in the best interest of the patient.
6. Please include a consent clause to the nurse passing on any comments made about the mask.
7. Please clarify what the post-participation options are.
8. Please check for typos.
9. Please include a statement about the tapu nature of the head
10. On page 2, it is incorrect to state that the person interested decides if it’s in the patient participant’s best interests – please amend the statement: ‘If you were not well enough to review the information sheet prior to receiving NIV therapy and your caregiver believes that it is in your best interest you may have already been given the study mask as part of your treatment.’
11. On page 2, please mention dry mouth as a risk.
12. On page 2-3, please discuss the appropriate ways in which a patient participant consents to CONTINUED participation in the study – they can decline to have the mask on and/or continued use of data already collected – the only option doesn’t need to be destruction of already collected data.
13. On page 5, the right to withdraw data is noted but doesn’t state what options are for continued use or otherwise. Please provide more detail about the type of data being collected – for example, participant hospital medical records for completion of adverse event reporting (if applicable).

CLINICIAN PISCF

1. Please provide a PIS for participating clinicians. Explain that they will receive training around participation in this study.

CASE REPORT FORM

1. Questions on this form are ill-suited to the patient participant and not intended to be completed by them so wording is inapt: “Compared to YOUR current NIV mask, how would you rate the investigation mask?” Please amend.

Decision

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

* 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).*
* Please update the study protocol, taking into account the feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).*

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| **2** | **Ethics ref:** | **21/NTA/91** |
|  | Title: | First-in-Human Study of XMT-1536 in Cancers Likely to Express NaPi2b |
|  | Principal Investigator: | Dr. Peter Chee Choong Fong |
|  | Sponsor: | IQVIA RDS Pty. Ltd |
|  | Clock Start Date: | 03 June 2021 |

Dr Peter Chee Choong Fong and Vivian Sun 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. XMT-1536 is a type of antibody drug conjugate; this means it has 2 parts that are joined together into one drug. The first part is an antibody that binds to NaPi2b (sodium-dependent phosphate transporter), a protein on the surface of the cells of the tumor. The second part is a cancer medicine that is attached to the antibody. When the antibody binds to NaPi2b, it carries the cancer medicine directly into the tumor cells to kill them. This is a Phase 1b/2 “First-in-Human” study.
2. This study is divided into three parts: dose escalation, dose expansion, and the pivotal cohort (UPLIFT). The first part of the study (dose escalation) has completed and is no longer enrolling.
3. The dose escalation phase of the study was conducted to test different doses of XMT-1536 and to find the highest dose of XMT-1536 that can be tolerated and that seems reasonably safe. The current dose of XMT-1536 that is found to be well tolerated and that seems reasonably safe is 43mg/m2. There is no placebo used in this study.
4. About 160 patients will be dosed in the second part (dose expansion) of this study.
5. Participants may stay in the study and continue dosing with XMT-1536 if their study doctor believe that they are benefiting from participation.
6. A Safety Review Committee (SRC) will monitor safety data and review the results of any analysis.

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 an update to this study means that it will just focus on the UPLIFT aspect of the study (part 3), which is regarding ovarian cancer.
2. The researcher clarified that they will ensure that the risk of anaemia in participants is minimised.
3. The researcher clarified that the risk of extra exposure to radiation for research purposes is reasonable.
4. The Committee queried why the researcher would not be providing participants the results from their genetic testing. The researcher responded that this is because it would equate to vast quantities of information that is irrelevant to their care.

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 update the study protocol to clarify that the tissue biopsy will not entail surgery or anaesthesia. Please specify what the tissue biopsy will entail. (*National Ethical Standards for Health and Disability Research and Quality Improvement* para 9.7).
2. Please provide some evidence of ACC equivalent, NZ-specific compensation. The currently provided letter with no sum or jurisdictional limits is insufficient. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 17.1).*
3. Please ensure that the international tissue bank complies with Chapter 15 of the *National Ethical Standards for Health and Disability Research and Quality Improvement*.
4. The Committee noted that there is information missing from the data management plan required to comply with Chapter 12 of the *National Ethical Standards for Health and Disability Research and Quality Improvement*, in particular who the data is going to be shared with and in what form (identifiable or de-identified) and for what purpose. Either include this information in the protocol or provide a NZ specific data management plan. Please refer to the [HDEC template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/hdec-data-tissue-management-template-oct2020.docx) for guidance.

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

MAIN PISCF

1. Please add IQVIA details on the front page as the local sponsor.
2. Please put the methodology and visits section into a table so that it is easier to understand for the participant.
3. Please remove all information that is not relevant to New Zealand participants, seeing you will only be doing part 3 of this study.
4. Please identify the central laboratory and tissue bank.
5. Please clarify where images are being sent overseas and that they will be de-identified.
6. Please refer to section 14.27 onwards of the *National Ethical Standards for Health and Disability Research and Quality Improvement* for guidance on the type of information required when discussing genetic testing.
7. The Committee noted that the compensation section refers to the Medicines NZ industry guidelines, which are only relevant if the sponsor is a member of that group. Please check this is the case, otherwise please reword.
8. Please provide the information about the tissue bank, required under chapter 15 of the *National Ethical Standards for Health and Disability Research and Quality Improvement*.
9. Please remove references to race and collecting race data. Instead, please refer to collecting ethnicity data *(*para 9.10 of the *National Ethical Standards for Health and Disability Research and Quality Improvement).*
10. Please amend the storage of data section to state a time limit rather than indefinite storage.
11. On page 16, please clarify that the study cannot stop for commercial reasons.
12. The data section is very dense and not easy to read. Please revise to include more headings and more information on some issues. Please remove repetition.
13. On page 11, please use the macron for Māori.
14. Page 12 – please include some risk numbers (e.g., one in 10) for the more serious side effects experienced
15. On page 14, please remove abstinence as a form of contraception. Please see the [HDEC template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc) for guidance.
16. Please revise the following statement on page 20, as it is an overstatement: “this will help make sure that information from this research is protected and can benefit Maori now and in the future”
17. Please clarify what is optional future unspecified research (FUR). Please put all optional biopsy and blood FUR into a separate PISCF, with the ability to consent to one or both, and only briefly mentioning it in the main PISCF, so as to avoid confusion. Please see the [HDEC template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/future-unspecified-use-tissue-piscf-template.doc) for guidance.

Optional FUR PISCF

1. Please ensure participants are informed about any optional FUR for data, and ensure that this complies with para 7.57 of the *National Ethical Standards for Health and Disability Research and Quality Improvement*.
2. Please include a time limit for the storage of tissue. Indefinite storage is not allowed.
3. Many of the sections in the optional tissue FUR CF are not relevant – please revise. E.g. advising the GP and withdrawal of information needs to be carefully tailored to this sub-study.

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 Forms, taking into account the suggestions made by the Committee.

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

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| **3** | **Ethics ref:** | **21/NTA/93** |
|  | Title: | (duplicate) GWAS of asthma in Niue Islanders |
|  | Principal Investigator: | Dr William Abbott |
|  | Sponsor: |  |
|  | Clock Start Date: | 03 June 2021 |

Dr William Abbott 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. A collection of 492 DNA samples from people of Niue Island ethnicity was obtained between 1997 and 1999. The purpose of the collection was to identify asthma susceptibility genes in the Niue Island population. 184 subjects had atopic asthma, 29 had non-atopic asthma, 220 subjects have never had asthma and there were 59 subjects in whom it was not possible to assign an asthma phenotype. There were 100 control subjects aged > 40 years who have never had either childhood-onset or adult-onset asthma. An aliquot of 3ug of this genomic DNA from each subject will be undertaken. The researcher will use a GSA array to type 749,000 SNP loci. Statistical analyses of the genetic data will be performed by a co-investigator (Dr David Duffy) who is an internationally recognised expert on asthma genetics.

Summary of resolved ethical issues

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

1. The Committee clarified that the researcher is submitting this application as a new application rather than seeking a reconsideration of the decision on his previous applications.
2. The Committee noted that the researcher is looking for a waiver of reconsent for children participants in the study who are now adults. The researcher argued for a waiver of consent on the basis that it would be impossible to trace over one hundred children who initially consented to partake in the research over 20 years ago. He referred to para 7.50 of the NEAC Standards which outlines practicality as a reason for granting a waiver of consent. He also noted that the potential harms of the study are balanced against the potential benefits of the study, noting that he could not see any serious consequences. Having regard to all of the criteria of Standards 7.50 – 7.56, the Committee agreed to grant the waiver of reconsent for child participants in the study who are now adults.
3. The Committee asked the researcher to clarify if he was seeking a waiver of consent for adult participants in this study or arguing that using a GSA array to type 749,000 SNP loci is consistent with the original consent for use of the samples. The researcher responded that he was relying on the latter. The Committee agreed with the researcher but nevertheless noted that there are other contextual factors involved now such as the age since the consent was taken, the fact that the participant information sheet (PIS) did not address extended periods of storage (or other matters which PISs would be expected to address today), and the potential for distress or dignitary harm.
4. On the other hand, the Committee noted that steps have been undertaken to mitigate these potential risks of harm, such as (1) the appointment of Associate Professor Colin Tukuitonga as a co-investigator who is Niuean and who has extensive knowledge and experience of working with Pasifika people; (2) obtaining thoughtful cultural advice (3) the provision of independent peer review; (4) the provision of a data and tissue management plan (albeit requiring some amendment, refer below). The Committed noted the support of the Niuean Government and considered that, having regard to the above-referred factors, in addition to the potential benefit of the study for Niueans, the potential harms of the study have been mitigated. The Committee agreed that a waiver of consent is not required because using a GSA array to type 749,000 SNP loci is consistent with the original consent for use of the samples and, overall, the nature, degree and likelihood of possible benefits outweigh the nature, degree and likelihood of possible harms.
5. The Committee queried the intellectual property claim from the Niuean government. The researcher clarified that this study would not generate any intellectual property, as a discovery cannot be patented,
6. The researcher clarified that the genetic analysis of the children’s tissue samples would not reveal any results that require informing the participant that they should seek medical attention. The participants are already aware that they have asthma.

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 amend the study documentation (protocol, data tissue management plan) to clarify that the genetic analysis will be undertaken in NZ not Australia as originally proposed.
2. The Committee requested that now that the genetic analysis is going to be performed in NZ the researcher think carefully about how the data will remain de-identified, for example who will be doing the de-identifying of the genetic analysis, how the study is going to work overall and how the co-investigator will be given access to the full data as well. Please amend study documentation accordingly.
3. The Committee noted that when submitting the study results to journals, the study data may be requested in order for a peer review to be completed. The researcher clarified that only de-identified data would be shared with journals. The Committee noted that de-identified data would be the bare minimum requirement – it would be preferable for the data to be anonymised before being shared with journals or not shared at all and an exemption sought from journal editors given the undertaking in the PIS that “samples will not be released to overseas scientists”. Please consider and clarify in the data management plan.
4. The Committee requested that the researcher clarify in the study documentation that the Niuean Government does not have an intellectual property claim over the study results.
5. Please update study documentation to note that Ag Research will be doing the genetic analysis.
6. Please provide a timeline for tissue destruction at the end of this study, as this was noted in the original PIS and consent. The Committee suggested a two-year time frame from the end of the study, and requested that the researcher give confirmation of the destruction of the samples in the final report.
7. The Committee noted that the protocol states there is not a risk of incidental findings and that this is inconsistent with the possibility of unexpected paternity findings. The Committee requested that the researcher amend the protocol to be in line with the NEAC Standards for incidental findings, to include having a plan for what will be done in this instance (e.g. non-disclosure).
8. The Committee requested that the co-investigator be named in the protocol.

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 study protocol, taking into account the feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).*
* Please update the data management plan to ensure the safety and integrity of participant data *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15).*

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

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| **4** | **Ethics ref:** | **21/NTA/94** |
|  | Title: | Auckland Sleep Surgery Study |
|  | Principal Investigator: | Mr Sumit Samant |
|  | Sponsor: |  |
|  | Clock Start Date: | 03 June 2021 |

Mr Sumit Samant and Mr James Johnston 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. Obstructive sleep apnoea (OSA) is characterised by repeated upper airway obstructions during the night. OSA is associated with excessive daytime sleepiness, lower health status and studies suggest obstructed breathing and snoring in sleep are independent risk factors for high blood pressure, heart disease, stroke and mortality. Thus, OSA is a serious and costly public health problem that is growing in prevalence because of population increases in both obesity and ageing.
2. Continuous positive airway pressure (CPAP) therapy is the current treatment of choice for patients with OSA. CPAP is effective in decreasing sleepiness and improves quality of life in patients with OSA. Treatment of OSA with CPAP is cost-effective if worn, but CPAP is poorly tolerated by many patients who find the mask and pressure claustrophobic and uncomfortable. OSA can be effectively treated but poor treatment compliance is a major clinical problem and thus many patients are under treated or not treated at all.
3. Upper airway surgery for OSA is widely used and reported in observational studies but there are few rigorous and randomized clinical trials to provide and validate these studies. The clinical effectiveness and cost effectiveness of this surgical intervention need to be validated.
4. This study is a randomised, controlled trial with a recruitment target of 102 participants. Participants with OSA who have failed standard OSA treatments will be randomised into two groups: Group 1 will receive reconstructive surgery of the upper airway and Group 2 will receive the standard non-surgical care for OSA. Participants will undergo follow-up for 6 months.
5. Study participants will be tested for OSA, daytime sleepiness levels, and quality of life improvements before the treatment and at 6 months follow-up.

Summary of resolved ethical issues

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

1. The Committee noted the peer reviewer’s comment regarding BMI and the potential for racial bias. The researcher responded that there is a potential bias there, and to mitigate this they are allowing a higher BMI in Māori and Pasifika patients in the inclusion criteria, so as not to exclude potential participants from these population groups. The Committee was satisfied that this seemed like a good strategy to proactively address this bias risk.
2. The researcher clarified that participants with an anatomical obstruction that are randomised to standard of care will have the opportunity to have the surgery after the study.
3. The researcher clarified that they will be hiring a study coordinator to manage the study.
4. The researcher confirmed that the medical monitor comments and no sponsor were errors in the form.

Summary of outstanding ethical issues

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

1. Researchers must conduct their research according to a suitably detailed protocol. The level of detail the protocol contains should be commensurate to the risk of the activity. Protocols must include all information that is relevant for the type of study (*National Ethical Standards for Health and Disability Research and Quality Improvement, paras 9.7-9.8*).
   * The Committee requested that the researcher provide a standard literature review and defendable justification of the study in the study protocol.
   * Please update the protocol to include a data and tissue management plan. Please see the [HDEC template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/hdec-data-tissue-management-template-oct2020.docx) for guidance.
   * Please update the protocol to provide information regarding:
     + the scientific basis of having different tests in the different arms
     + screening
     + how the qualitative part of the study will be undertaken e.g. who will complete the surveys, whether these are electronic.
     + how follow up will be done
     + what methods you will use to keep in contact with participants
     + serious adverse events
     + more detail about how cost-effectiveness part of the study will be done (put in PIS also)
     + more detail around the independent data safety monitoring committee
     + blinding – e.g. who will see the data and how the blinding will be done, by who, etc.
2. Please provide further detail in the protocol on the risk prediction model, if this is intended to be developed, and it will need to be explained to participants.
3. Please confirm whether cost-effectiveness analysis will be conducted, and if so detail the relevant data collection and methods in the protocol and explain this to participants.
4. Please confirm who and under what circumstances a fibreoptic assessment will be undertaken, and whether this is usual care or a study procedure.
5. Please remove identifying questions from questionnaires e.g. name, date of birth.
6. Please provide all questionnaires.
7. The Committee requested that the researcher reconsider the statement regarding there being no risk of stigmatisation, as this may not be accurate.
8. Participants must receive the information that a reasonable consumer, in that consumer’s circumstances would need to make an informed choice or give informed consent prior to their decision to participate in research (*National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.16)*
   * The Committee requested that the researcher ensures that consent for access to prior sleep studies and questionnaires is obtained and be specific when informing participants about these prior studies and questionnaires.
   * The Committee noted that forms completed by participants’ bed partners would make those people participants in the study. Please upload a PISCF for these participants.
9. Please ensure that all investigators and various people involved have undertaken GCP training.

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

1. Please describe the surgery with further detail, and include the risks of the study including the risks of surgery and the recovery period.
2. Please explain how participants will be tested for OSA.
3. Please provide more description of both arms of the study.
4. Please include a table of procedures.
5. Please clarify the duration of the follow up.
6. Clarify that they can withdraw from the study and further data collection, however the surgery will be permanent.
7. Please include more information regarding data and privacy, including what happens to data on withdrawal from the study and whether there will be any future specified or unspecified use of data. Please see the [HDEC template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc) for guidance.
8. Please remove statements that imply you already know what the outcome of the study will be. Do not presuppose benefit when presenting information to patients.
9. Please remove details about the researcher’s background from page 2, as it may suggest to potential participants that they should participate based on those qualifications.
10. Please provide more detail regarding inclusion and exclusion criteria and how potential participants will be screened for this study.
11. Please provide more detail regarding the questionnaires and how long they will take to complete.
12. Please include a statement acknowledging the tapu status of head for Māori participants.
13. In the consent form, please only refer to things which have already been discussed in the PIS.
14. In the consent form, only use tick boxes for truly optional things.

Decision

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

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| **5** | **Ethics ref:** | **21/NTA/83** |
|  | Title: | The Nitric Follow-up Study |
|  | Principal Investigator: | Dr John Beca |
|  | Sponsor: |  |
|  | Clock Start Date: | 17 May 2021 |

Dr John Beca, Associate Professor Debbie Long, Dr David Buckley, Claire Sherring, and Shelley Barlow were present via videoconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The study is a follow up to the Nitric Oxide on Bypass study for child participants who had open heart surgery, sometime between 2017 and 2021. The Nitric Oxide on Bypass Study researched how the effects of the inflammatory response can increase the chance of having complications after surgery and can slow down recovery.
2. The Nitric Follow-up Study aims to study children’s thinking skills and brain development after open heart surgery, up until they are five years old. The study will explore child, parent, cardiac surgery and paediatric intensive care treatment factors. The researchers will also look at how children show different levels of behaviour, communication, and physical skills across childhood.

Summary of resolved ethical issues

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

1. The Committee asked whether the researchers have finished recruitment of participants for the prior Nitric Oxide on Bypass study. The researchers confirmed this.
2. The Committee noted that genomic analyses of previously biobanked blood samples will not be undertaken as part of the study in New Zealand. The researchers did not collect these blood samples in New Zealand and acknowledged it is disappointing not to have this data; however, the decision was due to the high costs involved with undertaking this part of the study in New Zealand. The researchers noted that the study will still be valuable in terms of developmental outcomes. Further, there will be some New Zealand participants in the Australian cohort who will have had their blood samples collected, although those numbers will be significantly smaller than if it were able to be done in New Zealand.
3. The Committee asked whether the inflammatory markers are important for clinical care or whether these samples are taken at all. The researchers confirmed that these samples are not taken at all, are not part of clinical care, and are not helpful from a clinical care point of view.
4. The Committee asked if the information sheet for the prior Nitric Oxide on Bypass study which the Committee had previously approved, provided an option for parents to consent to samples, but that this was just not offered. The researchers confirmed this.
5. The Committee asked if there has been any unblinding for analysis and the researchers stated that this has not been done yet.
6. The Committee noted that parents may wish to know to which arm their children were assigned.. The researchers stated that they can give parents this information once results are available and at the stage of changeover between studies.
7. The Committee noted that by being part of the follow up study, there is an opportunity for participants to have early intervention and support for neurodevelopmental concerns. The Committee asked whether this would be an early flag or if the potential intervention relies on the in-person visit with the neuropsychologist once the participant is five years old. The researchers stated that the annual questionnaires will serve as an opportunity to flag at risk children for further assessment and early intervention. Further, there are some children who are already turning five years old because they were recruited earlier in the prior study. Those children will have already had four years of annual screening plus an in-person follow up so their in-person visit will serve as a flag for further intervention. The researchers also stated that the online screening questionnaires will be sent to the participants’ respective cardiac teams, plus any nominated family healthcare providers. If participants are already linked with other healthcare providers and parents would like the report to be sent to them, the researchers will provide that. The report includes recommendations of the areas where the child may need further assessment or other services.
8. The Committee asked if there had been any discussion with a Māori advisor for this study. The researchers confirmed this for both the current and prior study. Both studies were reviewed by an advisor at Auckland District Health Board.

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 noted that the researchers want to keep the Participant Information Sheet light because parents will already be familiar with information due to the prior study. However, the neurodevelopmental assessment is not currently described well. For example, it does not include information that the neurodevelopmental assessment is for two days. The Committee suggested that the researchers either create a separate information sheet which is focused on the neurodevelopmental assessment or include more information in the current Participant Information Sheet.
2. The Committee noted that there is a consumer engagement part of the study. There is currently no separate Participant Information Sheet for this. While it is mentioned in the Protocol, the current Participant Information Sheet lacks information. The researchers stated that the current description is just for expression of interest. If parents choose to participate in the consumer engagement part of the study, they will be consented separately. The Committee requested that this be submitted as an amendment once applicable with updated consent forms.
3. The Committee asked what the researchers would do if the questionnaires reveal information about the health of parents that may need assessment (such as from the Kessler Psychological Distress Scale). The researchers stated that they would be looking at this data as it came in, and flagging issues to talk to parents about. They also stated that there is a section in the report sent to family healthcare providers which flags for parental health as well. Please include this information in the Participant Information Sheet and clearly outline what data may be provided to family healthcare providers and what parents might be followed up by the study or offered referral.
4. The Committee requested that the researchers review and add more information to the Data Management Protocol. Currently, there are some sections missing. More information is required with regards to security procedures such as RedCap encryption, given that data will be transferred from New Zealand to Australia. Please also ensure that the Data Management Protocol is specific to the study and remove any generic template wording that is irrelevant, such as ‘all participants will provide consent’ – this is incorrect because parents/caregivers are consenting for the children.

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

1. Please elaborate on the difference between what will happen in terms of the study for the child and also for the parent.
2. Please include more information about what the parent questionnaires will be about because parents will be asked about themselves as well as their children.
3. Please include information about RedCap and that the data will be held outside of New Zealand by RedCap in Australia. Please refer to the [HDEC template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc) for guidance on what information to include regarding data.
4. Please make clear that as part of this study, the study records from the prior Nitric Oxide on Bypass will be accessed. Please also include this as an item on the Consent Form.
5. Please remove reference to mobile phones being used to provide consent. Please also be mindful of the current [NEAC Standards](https://neac.health.govt.nz/national-ethical-standards/part-two/7-informed-consent/) in terms of electronic consent guidelines *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.25 and 7.29)*.

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, para 7.15 – 7.17).*

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

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| **6** | **Ethics ref:** | **21/NTA/96** |
|  | Title: | Patient responses to oxygen therapy (PROT) |
|  | Principal Investigator: | Dr Tony Williams |
|  | Sponsor: | Fisher & Paykel Healthcare |
|  | Clock Start Date: | 03 June 2021 |

Dr Tony Williams, Jenny Han, Caitlin Chatfield, and Rima Song 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.

Rochelle Style declared a potential conflict of interest on the basis that she is a potential beneficiary of a trust which owns some Fisher & Paykel shares. The Committee decided that she was able to participate in the discussion but not advocate for an approval if other members were more inclined to decline.

Summary of Study

1. The aim of this observational study is to measure physiological therapeutic responses in 20 patients on oxygen therapy via a ventilator within the Intensive Care Unit (ICU) at Middlemore Hospital. In addition, data on related clinical outcomes will be collected. The information collected will be used to inform product development of future oxygen therapy devices.

Summary of resolved ethical issues

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

1. The Committee asked if this application was for the same as a study which was to be undertaken in Tauranga. The researchers stated the Tauranga study was a previous one that never proceeded. This application is for a different study and a different participant population.

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 noted that it may be unlikely to obtain prior informed consent from some participants given they are in an emergency situation requiring ventilation. The researchers referred to relying on participants’ families for agreement to participate. The Committee referred the researchers to Right 7.4 of the [Code of Health and Disability Services Consumers' Rights](https://www.hdc.org.nz/your-rights/about-the-code/code-of-health-and-disability-services-consumers-rights/). Given that the Participant Information Sheet states there is no benefit to participants involved, Right 7.4 cannot be argued. If there is no benefit, it is not permitted under New Zealand law for individuals to participate without providing their prior informed consent. The Committee confirmed that it is fine if patients are awake prior and can consent prior. Progressing the research relies on participants who can give prior informed consent. Please remove the information relating to family and guardians because they will not be involved.
2. The Committee noted that the Investigator’s Brochure states that the Physiologic Hospital Information Logger (PHIL) box is not a medical device and asked the researchers to confirm that whether it directs therapeutic decision making. The researchers confirmed that the PHIL box does not direct therapeutic decision making. The researchers will use all their standard monitoring to make decisions as they normally would. The PHIL box is for additional background recording of data. The Committee noted that the Protocol states that the data will be linked to clinical outcomes and the researchers stated they may provide this information to Fisher & Paykel Healthcare as part of the study data. Please make this clear in the Protocol, Participant Information Sheet, and in the data management information.
3. The Committee noted that the data management information in the Protocol and Participant Information Sheet does not currently meet the [NEAC Standards](https://neac.health.govt.nz/national-ethical-standards/part-two/12-health-data/).This is particularly for data linked to medical outcomes and how that is distinguished, and how identifiable data is de-identified, stored and accessed by others. The Committee recommended including this either as an improved data management section in the Protocol or by including a separate Data Management Plan following the [HDEC template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/data-only-management-template-oct2020.docx) (*National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15).*
4. The Committee asked whether the data gathered via the PHIL box will be used to build another machine in future. The researchers stated they potentially will do this in future and referred to a statement in the Participant Information Sheet which explains this. The Committee requested that this be explained more clearly, including a statement about how the researchers may use participant data for this purpose as it is expected future use of data.
5. The Committee noted that the Protocol is unclear as to whether device risk analysis has already been undertaken. Please upload this information on the Portal as it is currently not available.

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

1. Please state upfront why participants are being rushed to participate in the study. This information is currently halfway down page 2 and should be stated earlier and upfront.
2. Please remove reference to communicating significant incidental findings to participants’ general practitioners given that this study will not be looking at significant findings and the data is not about patient centred outcomes.

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

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

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| **7** | **Ethics ref:** | **21/NTA/101** |
|  | Title: | (duplicate) The CRITICAL-ACS Study |
|  | Principal Investigator: | Dr Philip Adamson |
|  | Sponsor: | University of Otago |
|  | Clock Start Date: | 03 June 2021 |

Dr Philip Adamson, Lorraine Skelton, and Richard Troughton were present via videoconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The purpose of this study is to compare a coronary artery computed tomography (CT) scan with an invasive coronary angiogram (ICA) to identify or exclude blockage of the coronary arteries in patients diagnosed with a suspected heart attack.

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 that it had considered the application at a previous meeting and that they were pleased to see the attention to revise and update the documentation to address most of its previous concerns in the new application.
2. The Committee asked whether there may be a potential delay in patients undergoing angiography while they consider participating in the study. The researchers stated they do not envisage the CT scan causing any delays. Participants who have an indication for emergency angiography and urgently need to be examined in a cardiac catheterisation laboratory will not be recruited or eligible for the study. Further, the likelihood of causing delays in provincial centres is small because these centres are already experiencing delays. The researchers expect that the study may in fact reduce the delays for provincial centres because approximately one third of patients in main centres using time in the catheterisation laboratory do not actually need an angiography. A CT scan will identify those who do not need an angiography, providing more availability to the regions. The researchers consider that the study is an opportunity to improve access for smaller centres who struggle to get patients within 72 hours. The Committee was assured by the researchers’ explanation and noted that the Participant Information Sheet satisfies this as well.
3. The researchers confirmed that the mention of blood samples in the previous application has been removed from the study.

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 requested clarification about the data linking for the study and the three datasets involved. The researchers stated that ANZACS-QI is a national register that collects routine data and does not allow for export of identifiable data, only anonymised data. ANZACS-QI provides National Health Index (NHI) numbers to Enigma, which then creates encrypted NHIs. These are then sent to the various data sources for data linking. VIEW provides data from the Ministry of Health to ANZACS-QI and NIHI provides the researchers with the de-identified dataset, limited to the data required for the study’s purposes. The researchers also noted there is a careful governance structure for privacy in the datasets. The Committee appreciated the effort and level of detail the researchers put into explaining the data linking in the Participant Information Sheet and following the template; however, the information is still currently difficult to understand and could be simplified and moved around to make it easier for participants to understand. The Committee recommended that the researchers:
2. simplify and edit this section of the Participant Information Sheet by separating out the three datasets and explaining as simply as possible what is involved in those processes
   1. Requesting to access to information about them and their heart attack from the ANZACS QI registry which collects this information on everyone who has a heart attack in New Zealand
   2. Collecting information about them related to this study in a special form held in a different part of the ANZACS QI registry.
   3. Requesting access to information about their future health and hospital visits through a University of Auckland ongoing research project which collects and links data from Ministry of Health datasets about people who have heart attacks and what happens to them over time (VIEW).
3. explain to participants that there are good governance processes, privacy considerations and safety about how the data is managed in each of these datasets.
4. explain to participants who will receive and analyse the data, and in what form (eg when Christchurch Heart Institute is involved.
5. confirm whether GP records and/or other hospital records will also be accessed (and if so, requesting access to these records is a study procedure).
6. ensure that the more detailed information about the processes is included in the Data Management Plan with more detail about the routine VIEW datasets clearly documented (the researchers explained that their request was for a study-specific extract from the routinely matched VIEW datasets. In the routinely data-linked VIEW process please outline the datasets (and/or variables/fields) that will be accessed. This can be a higher level of description of variables/fields and does not need to include every field, but should include, for example, pharmacy, mortality, hospitalisations etc.
7. specify the timeframes for the data linking, for example please make clear that it is for one year for the primary outcomes of the trial.

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

1. On page 4, the Christchurch Heart Institute (CHI) is mentioned for the first time and referred to in the coded data section. There is no other explanation of how the CHI is involved. Please amend and provide more information.

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, para 7.15 – 7.17).*
* Please update the data management plan to ensure the safety and integrity of participant data (National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15).

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

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| **8** | **Ethics ref:** | **21/NTA/102** |
|  | Title: | ITL-2002-CL-001: A Study to Evaluate NTLA-2002 in Patients with Hereditary Angioedema (HAE) |
|  | Principal Investigator: | Dr Hilary Longhurst |
|  | Sponsor: | Simbec-Orion |
|  | Clock Start Date: | 03 June 2021 |

Dr Hilary Longhurst and Courtney Rowse were present via videoconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This study will test an experimental drug, named NTLA-2002, that may potentially be used for the treatment of Hereditary Angioedema (HAE). NTLA-2002 is an investigational product because it has not been approved by the New Zealand MedSafe or other drug regulatory authorities. It is a first in human study using the very recently developed CRISPR/Cas9 gene editing system technology to delete the relevant gene. No gene insertion was being undertaken.
2. Up to 55 patients with HAE will take part in the study across New Zealand, Australia, the United Kingdom, Europe, and the United States. Approximately three to four patients will be from New Zealand.
3. There are two parts to this study, and participants are being asked to take part in the first part (Part 1).

Summary of resolved ethical issues

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

1. The Committee acknowledged the complexity of HAE, and the suffering involved for those with the disease. The researchers stated that there is a large variety of options for treatment for HAE. However, HAE involves unpredictable painful swellings and is a huge burden for those with the disease. Currently, there are treatment options to treat each individual swelling attack, but it can be difficult to access those treatments. Patients often need to have medication administered intravenously (IV). Subcutaneous options are available, but they do not work as effectively as IV administration.
2. The Committee noted that the Protocol mentions treatment of overdose. The Committee asked what the possible cause of this is, given that the medication is administered at a scheduled time and at a specified dose. The researchers confirmed that there is only one dose planned for this study. The researchers stated that it is a generic statement in the Protocol to clarify what would happen in the event a participant were to receive more than the planned dose.
3. The Committee asked if this is a single blinding study and who is to be blinded. The researchers stated that it will be the patient who is blinded because it is not feasible for the physicians to be blinded to the treatment given it is new.
4. The Committee queried how participants will be able to distinguish between an attack and allergy, given that sinus symptoms can mimic allergy. The researchers stated that they will not include any patients who have regular allergic attacks. Further, for allergies, the symptoms are more rapid and clinically different, so patients can recognise the difference.
5. The Committee asked whether participants could be compensated in future/once the study is complete if a treatment injury were to happen, given the long-term nature of treatment (removal of the gene). The researchers stated that the largest risk is the treatment itself (via the single IV infusion). The second largest risk is during the time of observation. However, as this is a new treatment, the researchers were unable to confirm that there are no long-term risks and it will be necessary to have longer term follow up.

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 asked the researchers to explain the recruitment process. The researchers stated that recruitment would largely be through clinics and patients’ associations. There are three centres in New Zealand that look after patients with HAE – Auckland, Wellington, and Christchurch. There is also a strong international patients association and an Australasian and New Zealand branch. The researchers have contacted those groups to gather preliminary views on the study. A patients’ meeting will also be held to discuss contacting patients and gather their opinions about the various options the researchers would like to offer through the study. The Committee asked if any preliminary work has been done with the patients’ associations with regards to their views of gene therapy. The researchers stated that they have only had informal discussions. There will be a meeting on the weekend of 4 September 2021 which will cover a discussion wider than the study but will ascertain opinions about this study’s approach. The Committee requested that more engagement with the participant group be undertaken.
2. The Committee asked the researchers for an update on the Gene Technology Advisory Committee’s (GTAC’s) assessment. The researchers stated they have made a submission to GTAC but are yet to have a meeting. The Committee advised that it cannot make a decision until the GTAC process is complete. There may be some ethical issues the Committee may wish to comment on after viewing GTAC’s decision and any advice. The Committee requested copies of any minutes or decision from GTAC once available. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 14.45).*
3. The Committee noted also that, because of the novelty of the CRISPR/Cas9 gene editing system technology it is taking a precautionary and conservative approach to this study, especially given the minimal guidance given in the NEAC Standards although the Committee noted the availability of guidance in other jurisdictions.
4. The Committee noted the genotoxicity report which characterizes the risk of potential off-target editing and unintended genotoxicity from genome editing with NTLA-2002. That report concluded there is limited risk at therapeutic doses, with no off-target editing or DNA structural variants detected in exonic protein coding DNA or on any cancer associated non-coding DNA. However, the full effect and impact of these changes in locations other than the Kallikrein B1 (KLKB1) gene are not known.
5. The Committee expressed concern that the CRISPR/Cas9 technology hasn’t been sufficiently explained to participants along with its risks (chiefly off-targetting and side-effects which may not become apparent for years) which would enable the potential participants to provide fully informed consent. The Committee mentioned the possibility of using a video to explain the CRISPR technology. The researchers stated they had considered including a link in the PIS to videos and sought the Committee’s opinion on including such videos. The Committee noted it would need to review the videos and, if the videos were updated/changed after study approval, the Committee would need to see them as an amendment.
6. The Committee also mentioned the possibility of using surveys to assess participants’ baseline genetic literacy and understanding of CRISPR genome editing (eg, the Genetic Literacy and Comprehension instrument (GLAC) and noted other methods for enabling participants to provide fully informed consent such as those mentioned in the study: “The Meaning of Informed Consent: Genome Editing Clinical Trials for Sickle Cell Disease Desine, Hollister et al.)
7. The Committee noted that proactive Māori consultation is required given there is a range of views on gene editing. It is important to understand the local context for Māori when undertaking this study. The Committee referred the researchers to Associate Professor [Maui Hudson's paper](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6470265/) and the [Royal Society of New Zealand's 2019 report](https://www.royalsociety.org.nz/assets/Uploads/Gene-Editing-Legal-and-regulatory-implications-DIGITAL.pdf) on genetic modification *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 3.8).*
8. The researchers also noted that there has been a lot of Māori consultation for this study and they hope to continue the dialogue. The researchers stated that for their previous study, they consulted with Dr Helen Wihongi and Associate Professor Maui Hudson. The recommendation/feedback was for the researchers to provide a full explanation of the benefits and to ensure the impact on whakapapa is fully explained within the Participant Information Sheet, but that they are aware that gene editing in the human domain is evolving and there is a high chance of recruiting Māori participants. The Committee acknowledged this and requested that this be explained better in the Participant Information Sheet. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 3.8).*
9. The Committee noted there is an item in the diary questionnaire regarding severity of attack; however, there is no description for participants to guide them in terms of how to determine whether an attack was ‘severe’, ‘mild’ etc. The Committee requested that the researchers include descriptions in the questionnaire to help participants answer the question.

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

1. Please provide more detailed information about what existing treatments are currently available for HAE.
2. Please split Part 1 and Part 2 so that they are not in the same Participant Information Sheet.
3. Please provide more information generally about the CRISPR technology. For example, the inclusion of a video to explain the technology and/or a survey to determine whether possible participants understand the technology. It is important to ensure participants can understand this novel technology and what the risks are.
4. Please include more information about and make clear the fact that the study does not involve insertion of any genetic material.
5. Please include a statement in the Consent Form so that participants can explicitly confirm they understand the technology and its specific application to them. For example, state ‘I understand that the study involves gene editing’ and add any other relevant information.

Decision

This application was *declined* by consensus, as the Committee did not consider that the study would meet the ethical standards referenced above. The Committee advised that it would welcome a new application once outstanding matters are resolved, including the GTAC process. The Committee requested that copies of any minutes for discussions with GTAC be provided with the new application. Catherine Garvey is available to be contacted to discuss other issues that were not able to be raised in this meeting, prior to this study being resubmitted for review.

## 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:** | 20 July 2021 |
| **Meeting venue:** | Zoom - <https://mohnz.zoom.us/j/9738756003> |

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.

The meeting closed at 5pm.