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| **Committee:** | ESOP Covid-19 Health and Disability Ethics Committee |
| **Meeting date:** | 04 September 2020 |
| **Meeting details:** | Review conducted online with no researcher present for discussion |

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|  | **Item of business** |
|  | New application20/NTB/193 |

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| **Member Name**   | **Member Category**   | **Appointed**   | **Term Expires**   | **Apologies?**   |
| Mrs Kate O'Connor-Chair | Lay (ethical/moral reasoning) | 14/12/2015  | 14/12/2018  | Present |
| Dr Peter Gallagher  | (health/disability service provision) | 22/05/2020 | 22/05/2023 | Present |
| Dr Devonie Waaka          | Non-lay (intervention studies)          | 18/07/2016  | 18/07/2019  | Present |
| Mrs Helen Walker | Lay (ethical/moral reasoning)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Patries Herst | Non-lay (intervention studies)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Sarah Gunningham | Non-lay (intervention studies), Non-lay (observational studies)  | 05/07/2019  | 05/07/2022  | Present |
| Ms Catherine Garvey | Lay (consumer/community perspectives)  | 19/03/2019  | 19/03/2022  | Present |
| Dr Kate Parker | Non-lay (intervention studies)  | 11/02/2020  | 11/02/2023  | Present |

## New applications

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| **1**   | **Ethics ref:**   | **20/NTB/193** |
|   | Title:  | COVID-19 Renin Angiotensin Aldosterone system (RAAS) blood pressure medication study |
|   | Principal Investigator:  | Dr Rinki Murphy |
|   | Sponsor:  |  |
|   | Clock Start Date:  | 14 August 2020 |

The review of this application was conducted online with no researcher present for discussion.

**Potential conflicts of interest**

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

**Summary of study**

1. A study to investigate whether people who regularly take a particular type of blood pressure medication (which acts on the renin angiotensin aldosterone system (RAAS)) increases or decreases the expression of the ACE2 protein in the nasal cells, which is involved in COVID-19 virus entry. The study will measure the expression of the ACE2 protein in nasal swabs collected for the purposes of COVID-19 testing, from people who are and who are not taking such blood pressure medications.
2. Participants will be selected to consent for such use of their nasal swabs, according to whether they were taking this medication and by whether they tested positive or negative. The study will investigate whether factors such as age, medical comorbidities or genetic variants affect the expression of ACE2 protein in nasal cells.

**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 further details in the protocol around data and tissue management, which should address the National Ethical Standards for Health and Disability Research and Quality Improvement Chapters 12 and 14.
2. The Committee requested an independent expert peer review as the document was unreadable.

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

1. The Committee stated to refer to the HDEC template (<https://ethics.health.govt.nz/guides-templates-forms-0>), particularly the inclusion of the updated data management and confidentially sections.
2. The email for HDC is now advocacy@advocacy.org.nz, please amend.
3. Please amend to state that data will be stored for 10 years, not 5.

**Decision**

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

1. 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).*

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| **Committee:** | ESOP Covid-19 Health and Disability Ethics Committee |
| **Meeting date:** | 07 September 2020 |
| **Meeting details:** | Via Zoom |

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|  | **Item of business** |
|  | New application20/NTB/216 |

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| **Member Name**   | **Member Category**   | **Appointed**   | **Term Expires**   | **Apologies?**   |
| Mrs Kate O'Connor-Chair | Lay (ethical/moral reasoning) | 14/12/2015  | 14/12/2018  | Present |
| Dr Peter Gallagher  | (health/disability service provision) | 22/05/2020 | 22/05/2023 | Present |
| Dr Devonie Waaka          | Non-lay (intervention studies)          | 18/07/2016  | 18/07/2019  | Present |
| Mrs Helen Walker | Lay (ethical/moral reasoning)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Patries Herst | Non-lay (intervention studies)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Sarah Gunningham | Non-lay (intervention studies), Non-lay (observational studies)  | 05/07/2019  | 05/07/2022  | Present |
| Ms Catherine Garvey | Lay (consumer/community perspectives)  | 19/03/2019  | 19/03/2022  | Present |
| Dr Kate Parker | Non-lay (intervention studies)  | 11/02/2020  | 11/02/2023  | Present |

## New applications

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| **1**   | **Ethics ref:**   | **20/NTB/216** |
|   | Title:  | Investigating the excretion of SARS-CoV-2 in saliva and faeces |
|   | Principal Investigator:  | Dr Brett Gilpin |
|   | Sponsor:  | Institute of Environmental Science and Research Ltd |
|   | Clock Start Date:  | 04 September 2020 |

**Potential conflicts of interest**

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

**Summary of study**

1. The aim of this study is to determine the timing and concentrations of SARS-CoV-2, or markers of SARS-CoV-2 infection, that are excreted in saliva and faeces of infected people, and to evaluate different methods for detecting potentially infectious people.

# Summary of resolved ethical issues

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

1. The Committee queried why Jet Park is the focus and if there are plans to roll-out testing to other areas of the country. The researcher responded that as Jet Park is the primary isolation facility, outside of community transmission, it is a consistent area where the presence of the virus could be detected in the waste, allowing the calibration for testing to determine how they correlate between cases and virus shedding.
2. The Committee asked if the intention is to assist in the monitoring of an emerging cluster. The researcher stated that short-term it could be used to pick up potential unknown cases in the community and inform further testing, and long term could monitor vaccine efficiency.
3. The Committee stated their concern that the participants would be a captive population due to the mandatory quarantine processes and asked the researcher how they would ensure participation is truly voluntary. The researcher responded that consultation with the staff at the facility has been undertaken to gauge willingness of the population. In addition, it would be made clear to the participant that declining the processes of the research activity will not affect their stay or care at Jet Park. The researcher also stated they will not give results to participants and will advise them it is only for the benefit of future monitoring.
4. The Committee queried the issues around language barriers, and even though translations can be provided, what process will be undertaken to determine what language barriers a potential participant requires assistance with. The researcher clarified that their first contact as part of their usual health check-up over the phone often identifies language barriers that need to be overcome, which would inform what help can be given. The researcher also stated that if there appears to be any confusion and no informed consent can be gained due to language barriers, they would not be followed up with.
5. The Committee queried how obtaining written consent will be managed due to the COVID-19 risk this poses with droplets. The researcher stated that participants would be provided with the information sheet and saliva pottle prior to them getting their nasopharangeal swab as part of the facility’s monitoring. The returned consent form will be put in a plastic sleeve which can be easily cleaned, and the pottle will be in a specimen bag. The Committee discussed whether bringing the saliva sample with them to their swab indicated a strong willingness to participate. The Committee noted to consider electronic consent.
6. The Committee noted the inclusion of children and stated that the age of consent is 16 in New Zealand, not 18 as outlined in the protocol. The Committee stated that minors (7-15) also need to provide assent in addition to parent’s consent. The researcher stated that they intend to exclude under 16s after discussion with the Committee and would add them as an amendment later if required.

**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 following issues in the application form that resulted in information being missing due to fields not being populated from incorrect answers:
2. Physical risks to participants
3. Compensation questions (to determine ACC v commercial insurance)
4. All sections about informed consent (crucial in what is essentially a captive population)
5. Consent of those unable to provide independent consent, and whether assent will be obtained where possible.
6. What steps will be taken to ensure there is no undue influence to participate, e.g. from other household members.
7. The Committee stated that due to the researchers storing identifiable information with potential linking, and this being research on COVID-19 which garners high interest and with high level privacy breaches in the past, more documentation around the careful management of data storage and protection is required.
8. The Committee stated that proxy-consent for adults who lacks capacity to consent for themselves is not legal in New Zealand. This will need to be removed from the protocol and outline this as an exclusion criteria.
9. The Committee asked for clarification regarding Appendix 7 which states “Currently AgResearch does not have Human Ethics approval for stage 2 and wants to use these samples under ethical approval given to ESR”. The Committee noted that if future use of samples or data is seeking approval, this would need to be made clear in the tissue management plan and participant information sheet what is happening to samples, if anything, beyond the study’s use.

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

1. The Committee stated to refer to HDEC templates for assent and PIS/CF and work through those headings ([https://ethics.health.govt.nz/guides-templates- forms-0](https://ethics.health.govt.nz/guides-templates-forms-0) ).
2. Please amend to add risk of security breach.
3. Please review and amend participant information and instruction sheets for lay- language.
4. Please add statement to reflect that while there is potential for this testing to be used in a commercial environment, the participant will not receive any direct benefits/financial reward of this from participating.
5. Please add information about incidental findings and testing for other respiratory infections as outlined in the protocol.
6. Please Include information on what happens if participants want to withdraw and what happens to their samples and information.
7. Please add an optional tick box in the consent form for the faecal sample collection.

**Decision**

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

1. 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).*
2. 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).
3. Please supply a data governance plan to ensure the safety and integrity of participant data (National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15).

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| **Committee:** | ESOP Covid-19 Health and Disability Ethics Committee |
| **Meeting date:** | 14 September 2020 |
| **Meeting details:** | Review conducted online with no researcher present for discussion |

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|  | **Item of business** |
|  | New application20/NTB/219 |

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| **Member Name**   | **Member Category**   | **Appointed**   | **Term Expires**   | **Apologies?**   |
| Mrs Kate O'Connor-Chair | Lay (ethical/moral reasoning) | 14/12/2015  | 14/12/2018  | Present |
| Dr Peter Gallagher  | (health/disability service provision) | 22/05/2020 | 22/05/2023 | Present |
| Dr Devonie Waaka          | Non-lay (intervention studies)          | 18/07/2016  | 18/07/2019  | Present |
| Mrs Helen Walker | Lay (ethical/moral reasoning)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Patries Herst | Non-lay (intervention studies)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Sarah Gunningham | Non-lay (intervention studies), Non-lay (observational studies)  | 05/07/2019  | 05/07/2022  | Present |
| Ms Catherine Garvey | Lay (consumer/community perspectives)  | 19/03/2019  | 19/03/2022  | Present |
| Dr Kate Parker | Non-lay (intervention studies)  | 11/02/2020  | 11/02/2023  | Present |

## New applications

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| **1**   | **Ethics ref:**   | **20/NTB/219** |
|   | Title:  | Unplanned admissions to the Wellington Hospital Intensive Care Unit before, during, and after New Zealand’s initial COVID-19 lockdown – a retrospective cohort study |
|   | Principal Investigator:  | Dr Paul Young |
|   | Sponsor:  |  |
|   | Clock Start Date:  | 01 September 2020 |

The review of this application was conducted online with no researcher present for discussion.

**Potential conflicts of interest**

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

**Summary of study**

1. The study plans to undertake a retrospective study to evaluate rates of unplanned Intensive Care Unit (ICU) admission before, during, and after New Zealand’s COVID-19 Alert level 4/3 lockdown. The study also seeks to describe the characteristics and outcomes of patients admitted to Wellington Hospital ICU during lockdown in comparison to historical controls.

**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 waiver of consent appears to be justified on the grounds of practicality described in the application, however please note that where a waiver is granted the Committee is required to be satisfied that there are "appropriate data management plans in place" and that the researchers have identified whether consultation with cultural or other relevant groups is require (NEAC Standards 7.47 and 12.29).
2. For assistance with what is required for data management please refer to the general principles for data in Chapter 12 of the Standards, and in particular the requirements for Researcher Data Guardianship at 12.15.

**Decision**

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

* please amend the Protocol to ensure that it meets the requirements of the Standards as they relate to data management. The Protocol should contain detail about how the data is stored (identifiable vs de-identified for example), who has access to it and in what form including the use to which the data will be put now and in the future, how long it will be stored for and where, and the security arrangements for that storage
* please provide confirmation of consultation, whether obtained as part of your locality review or otherwise.

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| **Committee:** | ESOP Covid-19 Health and Disability Ethics Committee |
| **Meeting date:** | 25 September 2020 |
| **Meeting details:** | Review conducted online with no researcher present for discussion |

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|  | **Item of business** |
|  | New application20/NTB/221 |

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| **Member Name**   | **Member Category**   | **Appointed**   | **Term Expires**   | **Apologies?**   |
| Mrs Kate O'Connor-Chair | Lay (ethical/moral reasoning) | 14/12/2015  | 14/12/2018  | Present |
| Dr Peter Gallagher  | (health/disability service provision) | 22/05/2020 | 22/05/2023 | Present |
| Dr Devonie Waaka          | Non-lay (intervention studies)          | 18/07/2016  | 18/07/2019  | Present |
| Mrs Helen Walker | Lay (ethical/moral reasoning)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Patries Herst | Non-lay (intervention studies)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Sarah Gunningham | Non-lay (intervention studies), Non-lay (observational studies)  | 05/07/2019  | 05/07/2022  | Present |
| Ms Catherine Garvey | Lay (consumer/community perspectives)  | 19/03/2019  | 19/03/2022  | Present |
| Dr Kate Parker | Non-lay (intervention studies)  | 11/02/2020  | 11/02/2023  | Present |

## New applications

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| **1**   | **Ethics ref:**   | **20/NTB/221** |
|   | Title:  | GlobalSurg-CovidSurg Week: Determining the optimal timing for surgery following SARS-CoV-2 infection |
|   | Principal Investigator:  | Dr Deborah Wright |
|   | Sponsor:  |  |
|   | Clock Start Date:  |  |

The review of this application was conducted online with no researcher present for discussion.

**Potential conflicts of interest**

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

**Summary of study**

1. The study is a prospective, observational multi-centre international cohort study investigating the optimal timing for surgery following SARS-CoV-2 infection. Mortality rates between patients preoperatively infected with SARS-CoV-2 and those presumed unexposed at the time of surgery will be compared in order to model key country level surgical indicators such as surgical volume, patient demographics and adverse outcomes.
2. By doing so the researchers hope to deduce which patients are at an increased risk of poor post-operative outcomes and contribute to modelling studies looking at the global burden of disease. All patients undergoing surgical procedures except excluded procedures at any participating hospital, including hospitals that have not admitted SARS-CoV-2 infected patients will be included. Data will be collected over a stipulated 7-day period, with a 30 day follow-up after surgery.

**Summary of outstanding ethical issues**

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

1. a.1.2. for noting: as this study intends to answer a specific research question (what is the optimal timing for surgery following SARS-COV-2 infection) and its results may change surgical practice, it is difficult to see how this could be categorised as an audit per current NEAC guidelines.
2. a.4.1. Please ensure all medical students and junior medical staff involved in this research are explicitly aware of the ethical requirements for data collection and management as per the NEAC National Ethical Standards 2019 and each locality's data management / privacy policy.
3. p.4.3.1. As this study involves the collection and use of Māori health data, Māori consultation would routinely be required. As the study is materially similar to CovidSurg, it is reasonable to apply the recommendations of the consultation undertaken for the CovidSurg study to the current research.
4. Please ensure it is clear how long the anonymised REDCap data will be kept. The correspondence from the University of Birmingham refers to 5 years, but the application refers to only 3 years (and 10 years at site).
5. Please ensure that both gender and ethnicity are collected in accordance with the New Zealand statistical standards (how ethnicity will be collected is unclear from the data collection form, and the term "ambiguous" is not appropriate when collecting gender).

**Decision**

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

* please address the outstanding ethical issues and update the study protocol if necessary.

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| **Committee:** | ESOP Covid-19 Health and Disability Ethics Committee |
| **Meeting date:** | 09 April 2021 |
| **Meeting details:** | Via Zoom |

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|  | **Item of business** |
|  | New application21/NTB/90 |

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| **Member Name**   | **Member Category**   | **Appointed**   | **Term Expires**   | **Apologies?**   |
| Mrs Kate O'Connor-Chair | Lay (ethical/moral reasoning) | 14/12/2015  | 14/12/2018  | Present |
| Dr Peter Gallagher  | (health/disability service provision) | 22/05/2020 | 22/05/2023 | Present |
| Dr Devonie Waaka          | Non-lay (intervention studies)          | 18/07/2016  | 18/07/2019  | Present |
| Mrs Helen Walker | Lay (ethical/moral reasoning)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Patries Herst | Non-lay (intervention studies)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Sarah Gunningham | Non-lay (intervention studies), Non-lay (observational studies)  | 05/07/2019  | 05/07/2022  | Present |
| Ms Catherine Garvey | Lay (consumer/community perspectives)  | 19/03/2019  | 19/03/2022  | Present |
| Dr Kate Parker | Non-lay (intervention studies)  | 11/02/2020  | 11/02/2023  | Present |

## New applications

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| **1**   | **Ethics ref:**   | **21/NTB/90** |
|   | Title:  | A Phase 1, first-in-human, randomized, double-blind, placebocontrolled, dose-finding study to evaluate the safety, reactogenicity, and immunogenicity of ReCOV, a recombinant 2-component SARSCoV-2 subunit vaccine for COVID-19, in healthy adult subjects |
|   | Principal Investigator:  | Dr Chris Wynne |
|   | Sponsor:  | IQVIA |
|   | Clock Start Date:  | 06 April 2021 |

**Potential conflicts of interest**

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

**Summary of study**

1. This first-in-human study of ReCOV will aim to assess the safety, tolerability and immunogenicity of two dose levels of ReCOV in healthy participants. A total of 100 participants will be enrolled in 2 separate age groups (18 - 55 & ≥56 – 80 years old), each consisting of 50 participants. Each age group will be further split into either a low dose cohort (20ug) or a high dose cohor (40ug). Each cohort will include 25 participants who will be randomised to ReCOV vaccine or placebo in a 4:1 ratio.
2. Participants will be enrolled in the study for up to 13 months, in which there will be a two-week screening period, a 21-day vaccination period, a 4-week double-blinded follow up period, followed by an open-label long-term follow up period up to 12-months-post-vaccination. Once participants have completed the double-blinded period up to Day 52, they will be unblinded and those who received ReCOV will automatically move into the open-label follow-up period, and those wo received the placebo will be allowed to exit the study.
3. Blood samples to measure the body’s reasponse to the vaccine will be collected at specific time points during the study, safety will be closely monitored, and any changes in health will be recorded.
4. The results will be used to inform further clinical development of ReCOV.

**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 raised its concern that people who participate in the trial will be excluded from the national rollout of the Government-approved vaccine programme. The Committee noted participants on the placebo arm would be particularly vulnerable for the study period. The Researcher explained that preclinical work suggests participants who receive the active vaccine would develop an immune response likely to be protective against Covid but agreed there was an ethical risk for the placebo participants. The Committee queried why a positive control design was not used. The Researcher stated they were interested in local reactions and that is best done with a placebo design.
2. The Researcher suggested that after six weeks participants could be unblinded and those that received placebo could exit from the study and receive the Government-approved vaccine. The Committee requested the Researcher amend the protocol to incorporate this change.
3. The Committee queried if a participant withdraws before the six-week period are they able to be unblinded. The Researcher confirmed they could and would be managed appropriately.
4. The Committee queried how the compensation would work with unblinding at six weeks, as participants on placebo would not be required to fulfil the full study duration. The Researcher stated as participants entered the study in good faith and would be randomised to placebo then it is appropriate, they receive the full compensation amount. The Committee agreed this was reasonable.
5. The Committee raised the possibility of ‘covid passports’ or an equivalent arrangement in the future where people that have been vaccinated may have less restricted access to travel and queried how participation in the study would affect that. The Researcher stated they were unaware of any imminent plans of this but would work around and manage as necessary.
6. The Committee queried why sentinel dosing was only used in one of the four cohorts. The Researcher explained that by the time the older cohorts will be dosed forty participants will have been fully immunised and it is unlikely an acute reaction would be in the older groups so the sentinel dosing in these cohorts was not necessary. Please include more information on this in the re-submission.
7. The Committee queried why the monitoring period for the sentinel dosing was six hours instead of 24. The Researcher explained they were not expecting any cardiac toxicity and ECG monitoring would not be required and the main risk would be a local reaction e.g. immediate anaphylactic shock. The Researcher agreed to consult the FDA guidelines on vaccines and could extend this if it is recommended.
8. The Committee noted the advertisements are not clear that this is a vaccine study and requested this be made explicitly clear.

APPLICATION FORM NOTES:

1. Several responses refer to ACS only; this application has a CCST lead. Please review for future applications.

TISSUE MANAGEMENT:

1. r.3.7. Provide a justification for the retention of mandatory tissue samples for 15 years after completion of the current study (particularly for those participants who have not consented to optional future use of samples). - r.3.12 states samples will be destroyed at the end of the study, which is at odds with r.3.7 (samples will be retained for 15 years after the end of the study) and b.4.5 – b.4.5.2 (samples will be used for future unrelated research). Please clarify what is intended.
2. The application form (b.4.5.2) states that optional future research will include research not related to the current study; the optional PISCF appears to restrict research to that related to SARS-COV-2. The DTMP provides no guidance. Clarify what is intended.
3. Please confirm that, should a participant withdraw from the main study, the Investigator specifically asks whether optional future research consent is ongoing.

DISSEMINATION OF RESULTS

1. p.2.9. states all participants will be sent a lay summary of study results. This is also reflected in the non-optional tick-box in the consent form. Participants should have the right to choose whether they wish to be informed of overall study results. Please ensure this is optional, and not a mandatory requirement for study participation.

CULTURAL ISSUES

1. p.4.2. Clarify whether the response provided covers both study sites; this appears to be specific to the Auckland site.

COORDINATING INVESITGATOR

1. The Scientific Peer Review letter lists Paul Hamilton as the CI, while Chris Wynne is listed as CI on the application form. Other parts of the application form refer to ACS and not CCST. Please clarify who the CI is for the current application.

PISCF

1. p1. Please use a simple, plain English lay title as the short study title for both PISCF documents. The current title uses technical terms not readily understood by lay participants.
2. p2. Change 'will help you body develop immunity' to 'may help' - 'will help' suggests known efficacy.
3. p3. Not all health research in NZ is reviewed by an HDEC. Please review and amend accordingly.
4. p5. Replace 'we cannot guarantee or promise that you will receive any benefits' with 'this study is not designed to provide you with any therapeutic benefits'. This is particularly important given participants are not permitted to receive approved COVID-19 vaccines.
5. p5. Delete the sentence regarding doctors' fees etc. being free - this is an absolute expectation for clinical research and should not be perceived as a potential benefit of study participation. - p6. State how much 'back-up participants' will receive as reimbursement.
6. p6. Many sentences in the ReCOV risk section appear to have been taken from the protocol with no simplification. The only subheading using appropriate language is the 'allergic reaction' paragraph. Please amend using simple, plain English. Where a medical or technical term is used, explain each term in lay language.
7. p5. The potential risks of receiving this vaccine (or placebo) instead of an approved vaccine should be clearly stated.
8. p7. Explain what happens if a participant withdraws from the study and wishes to receive an approved vaccine. Are there any potential interactions? Can the participant find out if they have received placebo or active vaccine?
9. p7. Sperm donation is not permitted for 6 months post dose, however there are no restrictions on egg donation despite the requirement for female participants to avoid pregnancy. Please provide a justification for this.
10. p9. Provide correct laboratory details for routine sample analysis for the Christchurch site, as per the DTMP.
11. p9. Clarify that only screening and safety samples will be identified with initials. There is no justification for other samples (immunogenicity etc) to be labelled with initials at any point.
12. p9. Delete 'also called the AIDS virus' after HIV. This term is well-understood by the lay public and the description is not accurate.
13. p10. Please amend the Māori contact information to be inclusive of the Christchurch site; discussing with Māori cultural support personnel in Auckland may not be culturally appropriate for South Island Māori.
14. p11. Add SARS-COV-2 to the list of notifiable diseases.
15. p11. No information has been provided about the intended use of data for future research; and whether this research will be restricted to research related to the current study. Please include.
16. p12. State specifically whether participants can find out whether they received active vaccine or placebo, should they elect to withdraw from the study.
17. Please include information advising participants of the possible implications of not receiving a Government-approved vaccine e.g. employment that requires a vaccine, restrictions on travel may be affected.

CONSENT FORM

1. The Committee requested an optional tickbox to allow participants to receive a lay summary if they choose.

FUTURE OPTIONAL RESEARCH PISCF

1. State clearly in lay terms whether the optional future research may involve genomic analysis (this is noted as a possibility in the DTMP). If genomic research is possible, this should be explained and the specific risks of genomic research included.

DTMP

1. Section 5. Include nasal secretions / nasal swabs (SARS-COV-2 testing).
2. Section 8.4. Define the limits of exploratory research for leftover tissue samples (related v unrelated).
3. Section 9.2. It seems unlikely that de-identified data will be retained for 18 months only. Review and amend accordingly.
4. Section 10.2. Correct text stating tissue use is restricted to mandatory uses (optional future use also applies in this study).
5. Section 11.1 Ensure the table encompasses both New Zealand sites (e.g. kotahitanga).
6. Section 11.1. The table references the donation of genetic samples. Please either delete of clarify what genetic samples will be collected.
7. Section 13. The continued analysis of tissue post-withdrawal is at odds with the application form, which states that tissue may be destroyed on withdrawal and only information gained from prior analysis will continue to be used. Please clarify what is intended.

**Decision**

This application was *declined* by consensus. The Covid-19 Health and Disability Ethics Committee has identified those ethical standard(s) and legislation(s) mentioned above have not been met by this application. The ethical standards are contained in the *National Ethical Standards for Health and Disability Research and Quality Improvement* and the *Standard Operating Procedures for HDECs*.

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| **Committee:** | ESOP Covid-19 Health and Disability Ethics Committee |
| **Meeting date:** | 29 April 2021 |
| **Meeting details:** | Review conducted online with no researcher present for discussion |

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|  | **Item of business** |
|  | New application21/NTB/108 |

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| **Member Name**   | **Member Category**   | **Appointed**   | **Term Expires**   | **Apologies?**   |
| Mrs Kate O'Connor-Chair | Lay (ethical/moral reasoning) | 14/12/2015  | 14/12/2018  | Present |
| Dr Peter Gallagher  | (health/disability service provision) | 22/05/2020 | 22/05/2023 | Present |
| Dr Devonie Waaka          | Non-lay (intervention studies)          | 18/07/2016  | 18/07/2019  | Present |
| Mrs Helen Walker | Lay (ethical/moral reasoning)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Patries Herst | Non-lay (intervention studies)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Sarah Gunningham | Non-lay (intervention studies), Non-lay (observational studies)  | 05/07/2019  | 05/07/2022  | Present |
| Ms Catherine Garvey | Lay (consumer/community perspectives)  | 19/03/2019  | 19/03/2022  | Present |
| Dr Kate Parker | Non-lay (intervention studies)  | 11/02/2020  | 11/02/2023  | Present |

## New applications

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| **1**   | **Ethics ref:**   | **21/NTB/108** |
|   | Title:  | A Phase1, first-in-human, randomised, double-blind, placebo-controlled, dose-finding study to evaluate the safety, reactogenicity, and immunogenicity of ReCOV, a recombinant 2-component SARS-CoV-2 subunit vaccine for COVID-19, in healthy adult sujects |
|   | Principal Investigator:  | Dr Chris Wynne |
|   | Sponsor:  | IQVIA |
|   | Clock Start Date:  | 22 April 2021 |

The review of this application was conducted online with no researcher present for discussion.

**Potential conflicts of interest**

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

**Summary of study**

1. This first-in-human study of ReCOV will aim to assess the safety, tolerability and immunogenicity of two dose levels of ReCOV in healthy participants. A total of 100 participants will be enrolled in 2 separate age groups (18 - 55 & ≥56 – 80 years old), each consisting of 50 participants. Each age group will be further split into either a low dose cohort (20ug) or a high dose cohor (40ug). Each cohort will include 25 participants who will be randomised to ReCOV vaccine or placebo in a 4:1 ratio.
2. Participants will be enrolled in the study for up to 13 months, in which there will be a two-week screening period, a 21-day vaccination period, a 4-week double-blinded follow up period, followed by an open-label long-term follow up period up to 12-months-post-vaccination. Once participants have completed the double-blinded period up to Day 52, they will be unblinded and those who received ReCOV will automatically move into the open-label follow-up period, and those wo received the placebo will be allowed to exit the study.
3. Blood samples to measure the body’s reasponse to the vaccine will be collected at specific time points during the study, safety will be closely monitored, and any changes in health will be recorded.
4. The results will be used to inform further clinical development of ReCOV.

**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 Participant Information Sheet and Consent Form (page 9) states that ‘HIV and SARS-CoV-2 are both ‘notifiable diseases’. Please add hepatitis B and hepatitis C to this list.

**Decision**

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

* please address all outstanding ethical issues raised by the Committee.

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| **Committee:** | ESOP Covid-19 Health and Disability Ethics Committee |
| **Meeting date:** | 07 May 2021 |
| **Meeting details:** | Review conducted online with no researcher present for discussion |

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|  | **Item of business** |
|  | New application21/NTB/117 |

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| **Member Name**   | **Member Category**   | **Appointed**   | **Term Expires**   | **Apologies?**   |
| Mrs Kate O'Connor-Chair | Lay (ethical/moral reasoning) | 14/12/2015  | 14/12/2018  | Present |
| Dr Peter Gallagher  | (health/disability service provision) | 22/05/2020 | 22/05/2023 | Present |
| Dr Devonie Waaka          | Non-lay (intervention studies)          | 18/07/2016  | 18/07/2019  | Present |
| Mrs Helen Walker | Lay (ethical/moral reasoning)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Patries Herst | Non-lay (intervention studies)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Sarah Gunningham | Non-lay (intervention studies), Non-lay (observational studies)  | 05/07/2019  | 05/07/2022  | Present |
| Ms Catherine Garvey | Lay (consumer/community perspectives)  | 19/03/2019  | 19/03/2022  | Present |
| Dr Kate Parker | Non-lay (intervention studies)  | 11/02/2020  | 11/02/2023  | Present |

## New applications

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| **1**   | **Ethics ref:**   | **21/NTB/117** |
|   | Title:  | A prospective cohort study to evaluate the immunogenicity of the Pfizer/BioNTech COVID-19vaccine in adults in New Zealand |
|   | Principal Investigator:  | Dr Michael Williams |
|   | Sponsor:  | Malaghan Institute of Medical Research |
|   | Clock Start Date:  | 29 April 2021 |

The review of this application was conducted online with no researcher present for discussion.

**Potential conflicts of interest**

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

**Summary of study**

1. The purpose of this prospective cohort study is to support the implementation of safe and effective COVID-19 vaccines for New Zealand populations. The study will assess immunogenicity in a subset of Pfizer/BioNTech COVID-19 vaccine recipients, with a focus on Māori, Pasifika, older adults ≥ 65 years, and those with co-morbidities.

**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 the recruitment process as the documentation is very light in terms of the approach. The researcher clarified that the approach for this research is very dependent on how the vaccine is rolled out in the country, and these are yet to be structured. After discussion, the Committee acknowledged that the researchers are in communication to liaise with relevant outreach groups and District Health Boards and are satisfied the vaccine rollout would not be disrupted. The Committee suggested that broader socialisation takes place using advertisement, and that the District Health Boards could refer participants to where to find more information about the study prior to their vaccination. The Committee requested a broad recruitment strategy to be documented as well as tailoring some of the recruitment material to be appropriate for the targeted groups.
2. The Committee queried if the Malaghan Tissue Bank used for depositing samples for future research was up to date as per the National Standards and requested transparency to meet standard 15.19. The researchers were unsure if the Tissue Bank complied with the current National Standards as it was approved prior to 2019. After discussion, The Committee and researchers agreed that having Malaghan store the samples for future specified research but not as part of the Malaghan Tissue Bank was acceptable.
3. The Committee requested clarification around when home visits will be made. If any are being performed under non-COVID-19 context, a safety plan with a tikanga protocol is required.
4. The Committee noted that date of birth is an identifier. Please amend to be year of birth in the database and keep date of birth in the source documents. Amendment to the data management plan is required.

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

Main PIS/CF

1. The Committee requested the removal of the ‘yes / no’ tick boxes from the consent form unless it is for a clause that is truly optional (i.e. the participant can answer ‘NO’ and still participate in the study).
2. The optional component of the main study for the food diary and stool sample needs its own optional consent statement.
3. Please separate the food diary and stool sample information under their own heading to make its inclusion clearer.
4. Please include how long each visit should take.
5. Please provide reassurance that there is no mandatory gene analysis as part of the main study.
6. Please make it clearer that you are targeting Māori and Pasifika.
7. Please ensure there is a footer with title, date and version number.

Sub-study PIS/CF

1. The Committee requested the removal of the ‘yes / no’ tick boxes from the consent form unless it is for a clause that is truly optional (i.e. the participant can answer ‘NO’ and still participate in the study).
2. Please provide more information around genes, the type of genetic studies being undertaken (i.e. individual genes or whole genome sequencing). Risks of genelinking and potential family identification should also be included.
3. Please include risks of sending samples and data overseas. The HDEC templates has wording that can be included (<https://ethics.health.govt.nz/guidestemplates-forms-0/participant-information-sheet-templates>).
4. Amend advocacy email to be advocacy@advocacy.org.nz.
5. Anything being tested beyond relevance to COVID-19 and immune response will need to be outlined in full as described in the protocol.
6. Please amend “chosen to participate” to “you are invited to participate”.
7. Please ensure there is a footer with title, date and version number.

**Decision**

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

1. Please address all outstanding ethical issues raised by the Committee.
2. 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).*
3. 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).*

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| **Committee:** | ESOP Covid-19 Health and Disability Ethics Committee |
| **Meeting date:** | 01 June 2021 |
| **Meeting details:** | Via Zoom |

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|  | **Item of business** |
|  | New application21/NTB/140 |

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| **Member Name**   | **Member Category**   | **Appointed**   | **Term Expires**   | **Apologies?**   |
| Mrs Kate O'Connor-Chair | Lay (ethical/moral reasoning) | 14/12/2015  | 14/12/2018  | Present |
| Dr Peter Gallagher  | (health/disability service provision) | 22/05/2020 | 22/05/2023 | Present |
| Dr Devonie Waaka          | Non-lay (intervention studies)          | 18/07/2016  | 18/07/2019  | Present |
| Mrs Helen Walker | Lay (ethical/moral reasoning)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Patries Herst | Non-lay (intervention studies)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Sarah Gunningham | Non-lay (intervention studies), Non-lay (observational studies)  | 05/07/2019  | 05/07/2022  | Present |
| Ms Catherine Garvey | Lay (consumer/community perspectives)  | 19/03/2019  | 19/03/2022  | Present |
| Dr Kate Parker | Non-lay (intervention studies)  | 11/02/2020  | 11/02/2023  | Present |

## New applications

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| **1**   | **Ethics ref:**   | **21/NTB/140** |
|   | Title:  | A first-in-human study of orally administered CoV2-OGEN1 in healthy subjects |
|   | Principal Investigator:  | Dr Christian Schwabe |
|   | Sponsor:  | Syneos Health |
|   | Clock Start Date:  | 28 May 2021 |

**Potential conflicts of interest**

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

**Summary of study**

1. CoV2-OGEN1 is an oral vaccine being developed for the prevention of COVID-19. This first-in-human (FIH) study will aim to assess the safety, tolerability and immunogenicity CoV2-OGEN1 in healthy participants.
2. A total of 45 participants will be enrolled into one of 3 cohorts, each consisting of 15 participants. Participants will receive 2 doses of CoV2-OGEN1, 14 days apart.
3. Participants will be enrolled in the study for up to 13 months, in which there will be a 2-week screening period, a 14 day vaccination period and a 12 month post-vaccination follow up period. At Day 43, the participant's immune response will be measured to determine if they have detectable immunity. If there is not a detectable antibody response, the participant will be administered a loading dose of CoV2-OGEN1 (not exceeding the maximum dose level). If there is still no detectable antibody response 4 weeks following the loading dose then the participant will be withdrawn from the study and allowed to receive the government-approved COVID-19 vaccine.
4. Blood samples to measure the body's response to the vaccine will be collected at specific time points during the study, safety will be closely monitored, and any changes in health will be recorded. The results will be used to inform further clinical development of CoV2-OGEN1.

# Summary of resolved ethical issues

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

1. The Committee queried if New Zealand was the only site. The researcher confirmed that New Zealand is the only site as the sample size of 45 makes another international site unnecessary. In addition, New Zealand has a unique comfort of low transmission in addition to a largely unvaccinated population.
2. The Committee queried what information is informing the dosing, and whether this is based on previous oral vaccine dosing information. The researcher responded that oral administration studies have been done before but not for COVID-19. The dosing is based on the animal and toxicity data for this vaccine.
3. The Committee queried if there is any interaction with the study vaccine and the approved vaccine in the government rollout. The researcher stated that there is no evidence of mixing vaccines as being unsafe, with examples overseas of different vaccines being combined in populations. There is no reason to believe that someone who did not get an immune response from the study vaccine would have a negative interaction with the approved vaccine.
4. The Committee stated that the $5million aggregate amount for 45 participants in a first in human trial is lower than expected. However, the Committee acknowledged the safety features and measures of this study reduce the risk as much as possible and were satisfied. The Committee suggested that this aggregate amount is increased in future to ensure in the event of an adverse event affecting multiple participants, the Sponsor can adequately cover compensation. They noted the primary risk to participants is being left with no cover should a Sponsor be unable to cover compensation beyond the insurance if an event would occur.
5. The Committee queried the one-hour observation post dose for non-sentinel cohorts. The researcher stated that the participants are unlikely to have a reaction to the vaccine and extending the observation beyond one hour is unlikely to add to the safety profile. Participants will be provided with contacts in the event of a reaction outside of observation. The Committee stated they will defer to SCOTT and their advice surrounding this.

**Summary of outstanding ethical issues**

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

1. The Committee queried the timing in terms of the booster dose and whether participants will be told in advance that they need a booster rather than wait until day 85 to know if they had an immune response. The researcher confirmed that they will know ahead of time whether the participant will need a booster dose and will inform the participants ahead of time, depending on when results are compiled. Four weeks following day 85, participants without an immune response will be discharged from the study. Participants will also be allowed to withdraw from the study at any time if they wish to instead receive the approved COVID-19 vaccine. The Committee noted there are discrepancies around timing in the protocol and participant information sheet and the schedule of doses is unclear. The Committee noted the visit summary did not adequately outline the above discussion. Please amend documentation to be clearer around these steps.
2. The Committee queried if the researchers have concerns about the safety of the in groups with booster doses, where the booster dose level has the potential to be higher than any dose level previously administered to any participants. The researcher responded that the animal toxicity studies had doses per kilogram of body weight in animals is vastly higher than doses that will be given to humans. Each dose will total 400 micrograms with a booster regardless of group. The Committee requested that investigators formalise in study documentation that the booster doses administered will not be higher than dose levels previously administered as first doses in the study.
3. Data and Tissue Management Plan (DTMP) mentions genetic samples in section 11 which contradicts the application form. Please remove this from the DTMP.
4. r.1.4 of the application form states an independent data safety monitoring committee will be utilised, however r.1.5. appears to describe an internal committee. The researcher clarified that this is internal and not independent. Please amend any relevant documentation.
5. The Committee queried contraception advice, with no restriction on egg donation noted. Please clarify and amend documentation if indicated.
6. The Committee requested all advertisement options make it clear that this vaccine is investigational.

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

1. Please make it clear that New Zealand is the only participating country.
2. Please clearly state that participation in the trial does not expedite access to receiving the approved COVID-19 vaccine that is available in the government rollout.
3. Please clarify what data the Sponsor is receiving, ensuring it is clear that no identifiable data is being sent as per the DTMP.
4. The analysis and storage of PK samples are discussed, but according to the schedule of events are not being collected. In addition, there is no mention of what happens to antibody blood samples or mucosal samples.
5. There is no mention that samples will be used for future related research (FRR) which is stated in the Protocol and Application form. The breadth of this must be clearly described such as no genetic testing, along with the mechanisms of withdrawal of samples from FRR if able.
6. Please make it clear that there is no evidence that the study vaccine is effective in preventing COVID-19.
7. Please clarify the time ranges at which information regarding immune response will be communicated to individuals, as these may be in advance of the scheduled study visits, and may influence decisions about on-going participation.

**Decision**

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

1. Please address all outstanding ethical issues raised by the Committee.
2. Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
3. Please update the study protocol, taking into account the feedback provided by the Committee. (*National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7*).

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| **Committee:** | ESOP Covid-19 Health and Disability Ethics Committee |
| **Meeting date:** | 06 July 2021 |
| **Meeting details:** | Via Zoom |

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| **Time** | **Item of business** |
| 11.00am | Welcome |
| 11.00am | New application21/NTB/181 |

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| **Member Name**   | **Member Category**   | **Appointed**   | **Term Expires**   | **Apologies?**   |
| Mrs Kate O'Connor-Chair | Lay (ethical/moral reasoning) | 14/12/2015  | 14/12/2018  | Present |
| Dr Peter Gallagher  | (health/disability service provision) | 22/05/2020 | 22/05/2023 | Present |
| Dr Devonie Waaka          | Non-lay (intervention studies)          | 18/07/2016  | 18/07/2019  | Apologies |
| Mrs Helen Walker | Lay (ethical/moral reasoning)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Patries Herst | Non-lay (intervention studies)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Sarah Gunningham | Non-lay (intervention studies), Non-lay (observational studies)  | 05/07/2019  | 05/07/2022  | Present |
| Ms Catherine Garvey | Lay (consumer/community perspectives)  | 19/03/2019  | 19/03/2022  | Present |
| Dr Kate Parker | Non-lay (intervention studies)  | 11/02/2020  | 11/02/2023  | Present |

## New applications

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|  **1**   | **Ethics ref:**   | **21/NTB/181**  |
|   | Title:  | VLA2001-304: A study comparing two versions of an experimental vaccine against COVID-19  |
|   | Principal Investigator:  | Dr Simon Carson  |
|   | Sponsor:  | PharmaSols  |
|   | Clock Start Date:  | 02 July 2021  |

Dr Simon Carson was present via videoconference for discussion of this application.

**Potential conflicts of interest**

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

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

# Summary of Study

1. The study is designed to assess and compare the ability of two vaccines, VLA2101 and VLA2001 to produce an immune response to SARS-CoV-2, the virus that causes COVID-19. VLA2001 has been designed to be effective against the Wuhan strain of SARS-CoV-2 and VLA2101 has been designed to be effective against the B.1.1.7 strain. The study will look at the immune response at various time-points for 1 year after vaccination. The study will also investigate the safety and tolerability of the vaccines in participants aged >55 (VLA2001) and in participants aged 12 and older (VLA2101).

# Summary of resolved ethical issues

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

1. The Committee queried why children aged 12-15 years are included in the study and receiving the vaccine in parallel with the adults. After discussion, it was clarified by the researchers that adults will be receiving the VLA-2001 vaccine first. With regard to the VLA-2101 vaccine, the Committee was assured that the difference in variants being tested is very minor and they anticipate that VLA2101 will have the same safety profile. The Committee was satisfied that the safety and efficacy was justified in this case.
2. The Committee asked how the recruitment through General Practices would work. The researchers outlined that they would have a cohort of referring practices who would identify potential participants and make the initial contact to give information about the study, and then with consent pass on contact details of interested potential participants for the researchers to then contact.

# Summary of outstanding ethical issues

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

1. The Committee noted that the advertisements used require amendment, as they are not clear that this trial involves investigational vaccines and should not make statements such as “COVID-19 Vaccine without the wait” as the vaccines have not been proven to be effective and are not approved. Further, the range of faces used are not diverse to reflect a New Zealand population.
2. The Committee queried if children are expected to have their own phone or computer access to be able to download the app and fill in the diaries, as some participants may not. The researcher said it is fine for a 12-year-old to have access to a device (like their parents) to fill in their own diary. The Committee suggested and the researchers agreed it was feasible to have a supply of devices to loan to participants who do not have access to a device, for the duration of the study.
3. The Committee asked the researchers to consider if both parents/guardians consent are required for those under 16 given this is a vaccine trial - of a vaccine untested in participants under 16.
4. The evidence of insurance certificate states it is a translation from Austrian-the wording is unusual for a clinical trial providing insurance for “bodily injury and property damage caused by ..manufactured or supplied products [and] operations carried out.” Please check that evidence of insurance is translated to follow standard wording expected in New Zealand, to provide ACC-equivalent compensation.

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

1. The Committee stated that instead of advising 12-year olds to inform their doctor they are sexually active in order to receive contraception advice; they should just have this advice included in their PIS to ensure that the information is given and to standardise the adolescent forms.
2. As future research is specified and only study-related, please remove the line “or for other medical and/or scientific research that is unrelated to the current study”. Further, please ensure the assent forms include information around future research.
3. Given the VLA-2101 vaccine variant is a very close relation of the vaccine that has already been tested in humans, VLA-2001, the Committee requested a simple lay explanation is provided early in the PIS on the variant and the expectation that it will share the safety profile of VLA-2001, as well as stating this is first in adolescents.
4. Adolescent participants should also be provided with a koha. The Committee discussed that it may be appropriate to provide this in the form of a voucher.
5. Please make it clear that the data transmitted from the eDiary app is deidentified/encoded.
6. Please include a statement to this effect in the PIS forms, confirming that the Sponsor will not have access to identifiable participant data through access to eDiary use.
7. Please include a statement notifying participants that the screening panels looks at notifiable diseases and identify which ones.
8. Please clarify participants access to the vaccine available in the government rollout and make it clear that participation in the trial does not exclude them from access to the approved vaccine.
9. Please add a statement to make potential participants aware that they should consider discussing with their employer of any potential issues their participation may have. This relates to the possible requirement in some roles for an employee to be vaccinated (with an approved vaccine).

**Decision**

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

1. Please address all outstanding ethical issues raised by the Committee.
2. Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
3. Please update the advertisements, taking into account the feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.12).*

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

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| **Committee:** | ESOP Covid-19 Health and Disability Ethics Committee |
| **Meeting date:** | 19 July 2021 |
| **Meeting details:** | Review conducted online with no researcher present for discussion |

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|  | **Item of business** |
|  | New application21/NTB/192 |

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| **Member Name**   | **Member Category**   | **Appointed**   | **Term Expires**   | **Apologies?**   |
| Mrs Kate O'Connor-Chair | Lay (ethical/moral reasoning) | 14/12/2015  | 14/12/2018  | Present |
| Dr Peter Gallagher  | (health/disability service provision) | 22/05/2020 | 22/05/2023 | Present |
| Dr Devonie Waaka          | Non-lay (intervention studies)          | 18/07/2016  | 18/07/2019  | Present |
| Mrs Helen Walker | Lay (ethical/moral reasoning)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Patries Herst | Non-lay (intervention studies)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Sarah Gunningham | Non-lay (intervention studies), Non-lay (observational studies)  | 05/07/2019  | 05/07/2022  | Present |
| Ms Catherine Garvey | Lay (consumer/community perspectives)  | 19/03/2019  | 19/03/2022  | Present |
| Dr Kate Parker | Non-lay (intervention studies)  | 11/02/2020  | 11/02/2023  | Present |

## New applications

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| **1**   | **Ethics ref:**   | **21/NTB/192** |
|   | Title:  | A Phase I, Open-Label, Dose-Escalation, Single Site Study to Evaluate the Safety, Tolerability, and Immunogenicity of a PIKA-Adjuvanted Recombinant SARS-CoV-2 Spike (S) Protein Subunit Vaccine in Healthy Individuals Aged 18-65 Years Old. |
|   | Principal Investigator:  | Dr Chris Wynne |
|   | Sponsor:  | Novotech (New Zealand) Limited |
|   | Clock Start Date:  | 14 July 2021 |

The review of this application was conducted online with no researcher present for discussion.

**Potential conflicts of interest**

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

**Summary of study**

1. The PIKA-Adjuvanted Recombinant SARS-CoV-2 Spike (S) Protein Subunit Vaccine is being developed for the prevention of COVID-19. This first-in-human (FIH) study will aim to assess the safety, tolerability and immunogenicity of the PIKA COVID-19 Vaccine in healthy participants.
2. A total of 45 participants will be enrolled into one of 3 cohorts, each consisting of 15 participants. Participants will receive 2 doses of the PIKA COVID-19 Vaccine, 7 days apart.
3. Participants will be enrolled in the study for up to approximately 7 months, in which there will be a 2 week screening period, an 8 day vaccination period and a 6 month post-vaccination follow up period. At Day 36, the participant's immune response will be measured to determine if they have detectable immunity. If there is not a detectable antibody response, the participant will be withdrawn from the study and allowed to receive the governmentapproved COVID-19 vaccine if they wish.
4. Blood samples to measure the body's response to the vaccine will be collected at specific time points during the study, safety will be closely monitored, and any changes in health will be recorded. The results will be used to inform further clinical development of the PIKA COVID-19 vaccine.

**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 dosing schedule was only one week apart whereas most of the other vaccines have three weeks apart. Please explain the rationale behind this.
2. The Committee queried whether a short time frame between doses could increase the possibility of an adverse reaction. Please comment on the safety of this.
3. The Committee noted the eight-week delay to inform participants that they are not sufficiently vaccinated is a long time period. Please comment on this and revise if necessary. Please ensure this is explained in the PIS so participants understand when they will be eligible for another vaccine if they do not receive sufficient vaccination in the trial.
4. Please clarify how recruitment from the database will be done and if material will be sent to potential participants (if so please provide this).

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

1. Please include information on the supplied thermometer.
2. Please include a statement in the PIS advising that the participant’s GP will be informed of their participation in the study (it is currently only on the consent form).
3. Page 3 of the PIS states that there is 24 hours of monitoring after sentinel doses; the application form / protocol states 48 hours. Please correct this.
4. Please simplify the exclusion criteria on page 5, either replacing or explaining medical / technical terms (myalgia, dyspnoea, encephalopathy, congenital, coagulation etc).
5. Page 7 includes a reference to ReCOV, administration, please correct this.

**Decision**

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

1. Please address all outstanding ethical issues raised by the Committee.
2. Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*

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| **Committee:** | ESOP Covid-19 Health and Disability Ethics Committee |
| **Meeting date:** | 26 July 2021 |
| **Meeting details:** | Via Zoom |

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| **Time** | **Item of business** |
| 2.00pm | Welcome |
| 2.00pm | New application21/NTB/196 |

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| **Member Name**   | **Member Category**   | **Appointed**   | **Term Expires**   | **Apologies?**   |
| Mrs Kate O'Connor-Chair | Lay (ethical/moral reasoning) | 14/12/2015  | 14/12/2018  | Present |
| Dr Peter Gallagher  | (health/disability service provision) | 22/05/2020 | 22/05/2023 | Present |
| Dr Devonie Waaka          | Non-lay (intervention studies)          | 18/07/2016  | 18/07/2019  | Present |
| Mrs Helen Walker | Lay (ethical/moral reasoning)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Patries Herst | Non-lay (intervention studies)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Sarah Gunningham | Non-lay (intervention studies), Non-lay (observational studies)  | 05/07/2019  | 05/07/2022  | Present |
| Ms Catherine Garvey | Lay (consumer/community perspectives)  | 19/03/2019  | 19/03/2022  | Present |
| Dr Kate Parker | Non-lay (intervention studies)  | 11/02/2020  | 11/02/2023  | Present |

## New applications

|  |  |  |
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|  **1**   | **Ethics ref:**   | **21/NTB/196**  |
|   | Title:  | PBI-0451-0001 (COVID-19): A Study to Evaluate PBI-0451 in Healthy Adults  |
|   | Principal Investigator:  | Dr.Mark Marshall  |
|   | Sponsor:  | Novotech (New Zealand) Limited  |
|   | Clock Start Date:  | 21 July 2021  |

Dr Mark Marshall, Ms Courtney Rowse, Dr Sharmin Bala, and Ms Olivia Dempster 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. PBI-0451 is being developed as an oral inhibitor of Coronaviruses (CoV), including the SARS-CoV2 that causes COVID-19 disease. This first-in-human (FIH) study will aim to assess the safety, tolerability and pharmacokinetics of single and multiple ascending doses of PBI-0451 in healthy participants.
2. Approximately 110 participants will be enrolled at a single site in New Zealand (NZCR). The study will be comprised of 3 parts: Part 1, Part 2 and Part 3. Part 1 will involve 4 cohorts (A, B, C & D), with each cohort consisting of 10 healthy participants who will be randomised to receive a single escalating dose of PBI-0451 or placebo in a 8:2 ratio respectively. Part 2 will involve 4 cohorts (E, F, G & H), with each cohort consisting of 10 healthy participants who will be randomised to receive 10 doses (once daily for 10 days) of PBI-0451 or placebo in a 8:2 ratio, respectively.
3. Part 3 will assess the potential drug-drug interaction (DDI) of PBI-0451 using Ritonavir and Midazolam, both of which are approved by NZ MedSafe and are being used in this study as they are known for their reactivity with other drugs. Part 3 will involve 3 cohorts (J, K & L), with each cohort consisting of 10 healthy participants. Participants in Cohort J will be randomised in an 8:2 ratio to receive a single dose of PBI-0451 or placebo. Participants in Cohort K will be randomised in an 8:2 ratio to receive 10 doses of PBI-0451 or placebo + Ritonavir. Participants in Cohort L will be randomised in an 8:2 ratio to receive 10 doses of PBI-0451 or placebo + Midazolam. The Part 3 doses will be determined based of Part 1 and Part 2 data.
4. Blood samples to measure the body's response to the study drug, and how quickly it is eliminated from the body (PK) will be collected at specific time points during the study, safety will be closely monitored, and any changes in health recorded.
5. The results will be used to inform further clinical development of PBI-0451.

**Summary of resolved ethical issues**

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

1. The Committee queried the intended use of the product if it is shown to be safe and effective and if it would be used in an emergency room setting or be available over-the-counter. The Researcher stated it would depend on the toxicity of the drug but imagined it would be in a primary care setting, although perhaps not over-the-counter.
2. The Committee noted the study is in three parts (single ascending does; multi ascending dose; drug-drug interaction) and requested comment on the risk profile of these compared to other first-in-human studies. The Researcher stated they believed the risk to participants would be lower as the drug targets viral proteases and is not aware of a human homologue. The Researcher stated animal studies did not show adverse events in the highest levels tested.

**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 the intention of the drug-drug interaction phase, and if the objective of this phase is to look for drugs that interact with each other or escalate effects. The Researcher confirmed that it is and explained that the animal shows show the drug is metabolised in the liver with almost none of it excreted in urine. The Researcher stated that other classes of drugs which are metabolised by this pathway in the liver should not be co-administered and are detailed in the Investigators’ Brochure. The Researcher stated there was uncertainty around the CYP3A4 pathway as rarely some people metabolise drugs down this pathway differently. The Researcher stated a lot of common drugs use this pathway, such as omeprazole. The Researcher stated one of the drugs to be given to participants in this phase is ritonavir which inhibits the pathway. The Researcher stated this would be to observe what happens to the study drug if the metabolising pathway is inhibited (e.g. will it accumulate to unsafe levels). The Researcher stated the second drug is midazolam in a low dose which does not inhibit the pathway but is processed via it. The Researcher stated there are two outcomes to observe here, firstly to determine what happens when two drugs metabolised via this pathway are in the system at the same time (i.e. will they both be metabolised) and secondly does the study drug have an effect on other drugs metabolised in the same pathway. The Researcher stated the latter of these may be inferred by this study but it is not a specific goal of it.
2. The Committee queried the clinical risk for participants in these scenarios and requested reassurance participation would not present a danger. The Researcher stated the dosing levels chosen are very low but enough to determine if the effect is present. The Researcher stated as the drug is not relevant to human biology and there is no human homologue the risk to human health is low.
3. The Committee queried why the drug-drug interaction phase was not being done the standard way, in which a single dose of study drug is given by itself and PK testing done, followed by dosing with ritonavir to steady state, followed by a second dose of study drug and second set of PK testing. The Researcher stated he believed by the time the third part of the study was being undertaken the Sponsor would have developed robust pharmacokinetic models and groups J, K and L would be tested against those models. The Committee requested a justification for not having participants act as their own control during this part of the study.
4. The Committee noted the value of the aggregate insurance compensation available is $5 million. The Committee noted that for110 participants it seems a low amount but was reassured that the study is staged in a way so that potential serious adverse outcomes would not all occur at once. The Committee queried the scenario for if the $5 million limit was reached and whether the company would re-insure or cover additional expenses itself. The Researcher stated he believed the latter but would seek confirmation.

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

1. The Committee requested the route of administration and doses of midazolam and ritonavir be added to the PIS. The Committee noted that protocol section 5.6 (Dosage and Administration) states that midazolam is a solution for injection whereas a different page states it is given orally. Please clarify this.
2. Please undertake a general revision to use lay language throughout the PIS. Medical and technical words should either be explained afterward or replaced with simple language.
3. Please include information on what a Holter monitor is so participants understand what will be attached to them. Please include any risks associated with using a Holter monitor.
4. Please remove references to ‘other Covid vaccines’ and experimental vaccines on page 9.
5. Please remove the references to mandatory genetic testing on page 12 as these are not applicable in this study.
6. Please remove the information on optional use of tissue for future unspecified research from the main PIS and present it in an optional FUR form.
7. Please remove the statement on optional use of coded data for future research. If deidentified information will be used in future research simply state so, explain what it will be used for and remove the mention of it being optional.
8. The side effects section uses ‘uncommon’ to describe rare side effects, please fix this.
9. Please include the uncommon, rare and severe side effects from midazolam.
10. Please insert a statement into the optional FUR PIS advising that there is no genetic testing.
11. Please remove the statement that participants may not receive a benefit as no clinical benefit is expected.
12. Please remove the reference to Medicines NZ if Pardes Biosciences is not a member.
13. Please convert the probability percentages on which drugs participants will receive to whole numbers (e.g. change 80% chance to 8 out of 10) and ensure the numbers given are accurate for the sentinel dosing.

The Committee requested the following additions to the DTMP:

1. Please add reference to optional secondary uses to section 4.
2. Nasopharyngeal secretions will be collected; please add to Section 5.
3. Please ensure future use of data is consistent between the PISCF and Section 8.4 of the DTMP
4. Future use of tissue is not referenced but is clearly intended; please address in Section 8.4.

**Decision**

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

1. 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).*
2. Please update the data and tissue management plan *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15; 14.16).*
3. Please confirm the ACC-equivalent insurance arrangements in the event the $5 million limit is reached. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 17.1).*

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

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| **Committee:** | ESOP Covid-19 Health and Disability Ethics Committee |
| **Meeting date:** | 03 August 2021 |
| **Meeting details:** | Review conducted online with no researcher present for discussion |

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|  | **Item of business** |
|  | New application21/NTB/212 |

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| **Member Name**   | **Member Category**   | **Appointed**   | **Term Expires**   | **Apologies?**   |
| Mrs Kate O'Connor-Chair | Lay (ethical/moral reasoning) | 14/12/2015  | 14/12/2018  | Present |
| Dr Peter Gallagher  | (health/disability service provision) | 22/05/2020 | 22/05/2023 | Present |
| Dr Devonie Waaka          | Non-lay (intervention studies)          | 18/07/2016  | 18/07/2019  | Present |
| Mrs Helen Walker | Lay (ethical/moral reasoning)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Patries Herst | Non-lay (intervention studies)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Sarah Gunningham | Non-lay (intervention studies), Non-lay (observational studies)  | 05/07/2019  | 05/07/2022  | Present |
| Ms Catherine Garvey | Lay (consumer/community perspectives)  | 19/03/2019  | 19/03/2022  | Present |
| Dr Kate Parker | Non-lay (intervention studies)  | 11/02/2020  | 11/02/2023  | Present |

## New applications

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| **1**   | **Ethics ref:**   | **21/NTB/212** |
|   | Title:  | A Phase I, Single-Site study to Test the Sensitivity and Specificity of the Orbis Quantitative Immunity for COVID-19 (QIC) Test in Detecting Levels of Anti-SARS-CoV2 IgG Antibodies in Vaccinated and UnVaccinated Airline Staff. |
|   | Principal Investigator:  | Dr Api Talemaitoga |
|   | Sponsor:  | Orbbis Diagnostics Limited |
|   | Clock Start Date:  | 28 July 2021 |

The review of this application was conducted online with no researcher present for discussion.

**Potential conflicts of interest**

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

**Summary of study**

1. The Orbis Arca is a benchtop device that can be deployed to non-laboratory points of need such as airports. The test has been designed to measure antibodies to SARS-CoV-2 (the virus that causes COVID-19) and hence provide confirmation of a person’s immune response to SARS-CoV-2. The test has been developed as a portable system with a rapid analysis time. The purpose of this study is to assess if the QIC test is accurate at detecting circulating antibodies to SARS-CoV-2 in vaccinated and unvaccinated airline staff.

**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 introductory email references the Participant Information Sheet, which should be attached.
2. Data Management Plan (S.12) incorrectly states "As data is collected anonymously, or has been anonymised, participants are unable to receive results of their individual study assessments." However, identifiable data (Study assessments, including laboratory test results, Participant medical records (if indicated) and the COVID-19 Immunisation Registry) are collected, and entered into the study databased in a coded manner. Please amend the management plan.
3. There is also reference to electronic consent, but if the first opportunity to provide the consent form is at the appointment then this will presumably be a hard copy.
4. Please provide an independent peer review; the Committee have only a letter stating the study has undergone rigorous internal review and has been reviewed by the Air New Zealand medical team. Please provide evidence of independent peer review from a suitably qualified expert in the field. Please see the HDEC website for guidance.
5. Please address the possible implications of a test finding where immune response is not as expected for a vaccinated worker. There are workers who are required to be vaccinated under the COVID-19 Public health Response (Vaccinations) Order. Presumably no immune response testing is done for anyone who has been vaccinated to test response other than in trials, so while it may be a small risk there would seem to be a potential risk that a person who is relying on being vaccinated to carry out their role does not carry anticipated immunity (that they would be unable to continue until that was remedied. This could also be important given the removal of need to isolate and quarantine for many crew in reliance on being vaccinated and the assumed antibody response this provides).
6. The Committee queried if there is also be a risk for those who are unvaccinated: first in terms of negative response (given the strong preference for vaccination for Air New Zealand staff) and secondly what are the implications of information suggesting a previously unknown prior infection, in terms of advice that should be given and steps that might be important.
7. The Committee queried why pregnant women could not participate.
8. Questionnaires for the phlebotomist and device operator have not been uploaded; please provide these for completeness.
9. The Committee queried what Air New Zealand’s role is other than providing a participant population. There is a risk of coercion if the email is on their letterhead; could perhaps attach the recruitment letter on the Orbis letterhead as well as the participant information sheet. If not (either way) the email should make clear that the response/info about who participates is not information that is provided to Air New Zealand.
10. Given the number of participants and that they are all from one employer, the Committee noted there should be caution around publications. Ethnicity data is being collected and could potentially identify a participant for example.

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

1. Remove reference to the MNZ compensation guidelines, as these do not apply to devices.
2. "Rights to Access Information" please ensure that this right extends to the results of the study test.
3. Include the address of the Sponsor on the first page.
4. In the Consent Form, add in a statement pertaining to the access of medical records from the participants employer (the airline), and add details of the implications of this to the main body of the sheet. Will the employer know that an employee has participated in this research? Will the employer be advised about immunity status?
5. Please ensure that the limits of the test are communicated, i.e. that the QIC test should not be used to diagnose or exclude acute SARS-CoV-2 infection, and that at this time, it is unknown for how long antibodies persist following infection (or vaccination) and if the presence of antibodies confers protective immunity.
6. Provide advice of both the walk-in clinic, and the pre-booking by appointment. For those that pre-book, state that they may be asked to give a duplicate sample.

**Decision**

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

1. Please address all outstanding ethical issues raised by the Committee.
2. Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
3. Please supply an independent peer review for the current version of the study protocol. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.26).*

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| **Committee:** | ESOP Covid-19 Health and Disability Ethics Committee |
| **Meeting date:** | 24 August 2021 |
| **Meeting details:** | Review conducted online with no researcher present for discussion |

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|  | **Item of business** |
|  | New application20/NTB/75/AM01 |

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| **Member Name**   | **Member Category**   | **Appointed**   | **Term Expires**   | **Apologies?**   |
| Mrs Kate O'Connor-Chair | Lay (ethical/moral reasoning) | 14/12/2015  | 14/12/2018  | Present |
| Dr Peter Gallagher  | (health/disability service provision) | 22/05/2020 | 22/05/2023 | Present |
| Dr Devonie Waaka          | Non-lay (intervention studies)          | 18/07/2016  | 18/07/2019  | Present |
| Mrs Helen Walker | Lay (ethical/moral reasoning)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Patries Herst | Non-lay (intervention studies)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Sarah Gunningham | Non-lay (intervention studies), Non-lay (observational studies)  | 05/07/2019  | 05/07/2022  | Present |
| Ms Catherine Garvey | Lay (consumer/community perspectives)  | 19/03/2019  | 19/03/2022  | Present |
| Dr Kate Parker | Non-lay (intervention studies)  | 11/02/2020  | 11/02/2023  | Present |

## Substantial Amendments

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| --- | --- | --- |
| **1**   | **Ethics ref:**   | **20/NTB/75/AM01** |
|   | Title:  | Australasian COVID-19 trial (ASCOT): A multi-centre RCT to assess clinical, virological and immunological outcomes in patients with SARS-CoV-2 infection (COVID-19) treated with lopinavir/ritonavir and/or hydroxychloroquine compared to standard of care. |
|   | Principal Investigator:  | Dr Susan Morpeth |
|   | Sponsor:  |  |
|   | Clock Start Date:  |   |

The review of this application was conducted online with no researcher present for discussion.

**Potential conflicts of interest**

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

**Summary of study**

1. This study is an open label randomised controlled trial of unproven treatments for pandemic coronavirus infection among people unwell enough to need admission to hospital, but not so unwell that they need intensive care. Consenting participants will be randomised to either lopinavir-ritonavir (an anti-viral used to treat HIV), hydroxychloroquine (used in autoimmune diseases), both of these agents in combination, or the current standard of care. The study will be carried out at multiple sites across Australia and New Zealand. The study will see whether either or both of these potential treatments will reduce the risk of needing intensive care or death from pandemic coronavirus infection.
2. This amendment is being made in order to add a convalescent plasma domain to the study protocol. This means that patients will have the option to be randomised to receive either standard supportive care, or convalescent plasma (plasma obtained from people who have recovered from COVID-19, containing antibodies to SARS-CoV2). In addition, the amendment now allows for enrolment of patients who are not competent to provide informed consent if their family members believe that they would wish to participate were they able to do so.

**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 stated it did not accept that randomisation based on chance for an opportunity to receive the intervention constituted the best interests of the individual and stated approval at this stage would be for consenting participants only.

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

1. Please adapt the data section from the PIS template available on the HDEC website. Include information on primary and secondary uses of data, that the study is an Australian-New Zealand collaboration and data will go overseas.
2. Please simplify technical / medical language for a lay audience.
3. Please include a lay-friendly explanation of what genes are, that these are shared between family and the implications for Māori.
4. Please include an explicit statement in the PIS that this is not currently an approved treatment in New Zealand.
5. Please include any relevant information alongside the statement that the intervention has been used overseas (e.g. how many people it has been tested in) along with the caveat that it is unknown whether it is beneficial.
6. Please add the CI’s direct contact number

**Decision**

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

1. Please address all outstanding ethical issues raised by the Committee.
2. Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
3. Please provide a justification that complies with Right 7(4) of the Health and Disability Consumers code demonstrating that participation in the standard of care arm of the trial would be in every individual’s best interest.

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| **Committee:** | ESOP Covid-19 Health and Disability Ethics Committee |
| **Meeting date:** | 26 August 2021 |
| **Meeting details:** | Review conducted online with no researcher present for discussion |

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|  | **Item of business** |
|  | New application21/NTB/224 |

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| **Member Name**   | **Member Category**   | **Appointed**   | **Term Expires**   | **Apologies?**   |
| Mrs Kate O'Connor-Chair | Lay (ethical/moral reasoning) | 14/12/2015  | 14/12/2018  | Present |
| Dr Peter Gallagher  | (health/disability service provision) | 22/05/2020 | 22/05/2023 | Present |
| Dr Devonie Waaka          | Non-lay (intervention studies)          | 18/07/2016  | 18/07/2019  | Present |
| Mrs Helen Walker | Lay (ethical/moral reasoning)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Patries Herst | Non-lay (intervention studies)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Sarah Gunningham | Non-lay (intervention studies), Non-lay (observational studies)  | 05/07/2019  | 05/07/2022  | Present |
| Ms Catherine Garvey | Lay (consumer/community perspectives)  | 19/03/2019  | 19/03/2022  | Present |
| Dr Kate Parker | Non-lay (intervention studies)  | 11/02/2020  | 11/02/2023  | Present |

## New applications

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| --- | --- | --- |
| **1**   | **Ethics ref:**   | **21/NTB/224** |
|   | Title:  | Immunity and Molecular studies of SARS-CoV-2 infection and COVID19 vaccination |
|   | Principal Investigator:  | Dr Anna Brooks |
|   | Sponsor:  | University of Auckland |
|   | Clock Start Date:  | 17 August 2021 |

The review of this application was conducted online with no researcher present for discussion.

**Potential conflicts of interest**

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 better understand the immune response following SARS-CoV-2 infection including measuring changes in immune cells and investigating the biological and molecular mechanisms underlying Long COVID symptoms.
2. The researchers aim to determine immune cell signatures (including immunity to COVID-19) and protein and molecular signatures within blood components (serum/plasma/cells) of Long COVID individuals compared with healthy controls and determine whether such signatures change following the course of COVID-19 vaccination.
3. In addition, the study will characterise plasma proteins and immune cells i.e., their function and molecular changes over time, in samples from individuals with Long COVID or a recent onset Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) - like condition (even if the cause is unknown), irrespective of vaccination status.
4. As New Zealand has largely been free of COVID-19, this puts the study in a unique yet urgent position to track immunity markers in those that were infected but have not been vaccinated.
5. This will also include a group of people who are experiencing post-viral symptoms without a firm diagnosis that they experienced COVID-19. These studies will seek to determine whether immune markers can accurately identify past infection as well as track longevity and robustness of the immunity induced in those that experience ongoing post-viral symptoms.

**Summary of outstanding ethical issues**

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

1. The Committee queried how the current outbreak would affect the study design (i.e. having participants have blood drawn at the University). Please revise the protocol as necessary.
2. The Committee queried the relationship with MWC/06/10/134 and any plans for data / tissue sharing. Please clarify.

Protocol:

1. The definition of 'healthy controls' appears to be anyone who does not have a terminal illness (f.2.1); this is not the usually accepted definition for clinical trials. ‘Severe clinical comorbidities’ are stated to be exclusionary in the application form, but there is no documentation of this in the eligibility criteria. A more accurate description would be 'no history or evidence of previous or current COVID-19 infection, ME/CFS, or post-viral syndrome'. Please clearly delineate the control population.
2. The protocol objectives relate specifically to long COVID, previous COVID infection, and COVID vaccination. It is unclear why confirmation of previous infection is not required for the 'COVID' group at study enrolment. Please clarify how previous COVID infection will be determined objectively in those with 'presumed' infection, and which analysis population participants enrolled as long-covid / previous infection but with no objective evidence of infection will be included in. All analysis populations should be clearly delineated in the protocol.
3. The rationale for including those with ME/CFS but no COVID exposure is unclear. The PISCF suggests antibody testing will be performed on-study to assess whether long-covid symptoms are due to COVID infection or not; this is not discussed in the protocol.
4. There is brief mention that PCR testing may be carried out in the event of community COVID transmission; provide further detail about when this would be undertaken and make provision for this in the eligibility criteria.

Advertisement

1. Please clarify how will people know whether they have had exposure to Covid-19 within the past 28 days.

Pre-screening Questionnaire:

1. Date of birth is requested twice, please correct this.

Questionnaire for blood donations:

1. The purpose of the consent section is unclear; explain when this form will be completed and why 'consent to be contacted to participate in this research' is sought after study-specific questions are asked.

On-study questionnaire:

1. Please clarify why identifiers are required for the on-study questionnaires. The PISCF states that 'when we download your data to do research, it will not contain your name of other identifying information'. Does this mean some of the information in the questionnaires (which include name, email address, etc) are not downloaded?
2. Please explain whether all sections of the questionnaire are intended to be completed by all cohorts.
3. Many of the medical conditions listed are significant co-morbidities (see point above re 'healthy controls'). Will any responses preclude the respondent from further study participation? Please clarify.
4. Many of the symptoms noted are common in the general population. There does not appear to be a distinction between symptoms that participants experienced prior to their confirmed or presumed COVID illness, and those experienced only after the diagnosis. Clarify how this information in captured.

PISCF:

1. The 'purpose of the study' section may be clear to those with long covid or CFS but is unlikely to mean much to the 'healthy control' group. Please review and simplify.
2. Please explain the possibility of long Covid participants having a worse outcome after receiving the vaccine.
3. Please explain in lay terms what DNA is and the breadth of this analysis (i.e. that only fragments of DNA will be analysed, not the individual's whole genome).
4. Please re-write 'who can take part in the study' in lay language.
5. Please give an estimate of the time required for the consent visit, blood donation, and questionnaires.
6. Please explain what is meant by 'Additionally, irrespective of vaccination, you could donate further blood samples for the ongoing longitudinal study of long COVID if you wished' (p3). This has no context for those participants not in a long COVID study.
7. Please make it clear whether any of the tests undertaken are notifiable (the protocol allows for PCR testing in the event of community transmission; this has mandatory reporting obligations).
8. Please state clearly that future research will be restricted to that directly related to COVID-19, and clarify whether this may include genetic research.
9. Also make it clear whether the results of future research will be available to participants.
10. Access to identifiable information is discussed in the first paragraph of the deidentified section.
11. Please describe future uses of data; the application form states that deidentified data will be shared with other researchers for future research.
12. Please state that data will be sent overseas.
13. Include risks of privacy breach and of sending data overseas.
14. GP notification regarding results of clinical significance should be mandatory - amend accordingly.
15. The application states sending tissue overseas is optional; this should be reflected in the consent clauses.
16. Participants are offered a tikanga appropriate disposal of tissue even if overseas which does not seem realistic. Please revise this.
17. Is the retention of tissue for 10 years solely for study related purposes. This is optional, but clarity around study related vs possible future research would be good (DTMP does say no future unspecified research).
18. State whether ME/Long Covid participants without a previous positive result for COVID will be informed of the positive result, and any implications of this. Is it necessary to consider that negative testing may still not be conclusive, and managing that information for participants also? This is in the protocol is not clear in the PIS. Please revise.
19. Please clarify the statement “The study will be active as long as the researchers and participants continue to learn from these data (i.e. we will recruit over the next three years).”
20. Please clarify in the PIS who has finger prick samples.
21. The PIS states that the surveys can be done in parts, not all in one sitting. Clarify if data is only uploaded once the whole survey is complete, or with each entry.

DTMP:

1. Section 4: Please address optional uses of data (data linking) and tissue (long term storage; sending tissue overseas).
2. Section 5: Please review and delete assessments not conducted as part of the study.
3. It would be helpful to have more information about overseas centres where tissue might be sent although for future related research it state collaborators are not yet known. Data is held at Te Ira Kawai but not tissue, which is held at named labs at the Universities of Auckland and Otago.
4. Data linking is optional but there is not enough information to address this. Several potential data sources are named in the protocol (sec 8.6) but it is not clear whether this is a one off (for purposes that should be clearly stated) or an ongoing intention to access data, and what data.

**Decision**

This application was *declined* by consensus. The Covid-19 Health and Disability Ethics Committee has identified those ethical standard(s) and legislation(s) mentioned above have not been met by this application. The ethical standards are contained in the *National Ethical Standards for Health and Disability Research and Quality Improvement* and the *Standard Operating Procedures for HDECs*.

* 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 DSMC. (*National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.25*).
* Please update the advertisements, taking into account the feedback provided by the Committee. (*National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.12*).
* 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*).

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| **Committee:** | ESOP Covid-19 Health and Disability Ethics Committee |
| **Meeting date:** | 10 September 2021 |
| **Meeting details:** | Via Zoom |

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| **Time** | **Item of business** |
| 10.30am | Welcome |
| 11.00am | New application2021 EXP 10976 |

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| --- | --- | --- | --- | --- |
| **Member Name**   | **Member Category**   | **Appointed**   | **Term Expires**   | **Apologies?**   |
| Mrs Kate O'Connor-Chair | Lay (ethical/moral reasoning) | 14/12/2015  | 14/12/2018  | Present |
| Dr Peter Gallagher  | (health/disability service provision) | 22/05/2020 | 22/05/2023 | Present |
| Dr Devonie Waaka          | Non-lay (intervention studies)          | 18/07/2016  | 18/07/2019  | Present |
| Mrs Helen Walker | Lay (ethical/moral reasoning)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Patries Herst | Non-lay (intervention studies)  | 22/05/2020 | 22/05/2023 | Present |
| Dr Sarah Gunningham | Non-lay (intervention studies), Non-lay (observational studies)  | 05/07/2019  | 05/07/2022  | Present |
| Ms Catherine Garvey | Lay (consumer/community perspectives)  | 19/03/2019  | 19/03/2022  | Present |
| Dr Kate Parker | Non-lay (intervention studies)  | 11/02/2020  | 11/02/2023  | Present |

## New applications

|  |  |  |
| --- | --- | --- |
| **1**   | **Ethics ref:**   | **2021 EXP 10976** |
|   | Title:  | Immunity and Molecular signatures of COVID-19 and post-viral conditions |
|   | Principal Investigator:  | Dr Anna Brooks |
|   | Sponsor:  | University of Auckland |
|   | Clock Start Date:  | 07 September 2021  |

Dr Anna Brooks was present by videoconference for discussion of this application on 10 September 2021.

**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 better understand the immune response and associated immune dysregulation that may occur following viral infections, specifically, SARS-CoV-2. The study aims to improve understanding of the underlying disease mechanisms and immunology of Long COVID and other post-viral conditions.

**Summary of outstanding ethical issues**

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

1. The Committee queried how Pasifika and Māori communities will be engaged with given their experiences with the outbreaks. The researcher responded that there are outreach researchers at Victoria University they can work with and expand for targeted recruitment, however at this stage it will only be self-referral. The Committee requested that translated documents are offered.
2. The Committee noted their concern with the crowd-funding money, and the undue influence this could potentially have as participants could have donated money for their own participation. The Committee stated that donors should not be included in the qualitative component of the study and this should be screened for. Further, any prominent/named people part of the crowd-funding campaign should be excluded from the research to avoid any potential conflict of interests. This is to ensure the integrity of the science is protected.
3. The Committee stated that if the finger-prick option does not allow for the complete set of tests that a venous blood draw would provide, this needs to be clear that this limits their participation and results from the research.
4. The Committee stated that there needs to be a clear plan as well as managing expectations in the likely circumstance where members of the research team are asked for advice from potential or enrolled participants about receiving a COVID-19 vaccine. It is important that expectations are managed from the beginning of the participant journey that the researchers cannot provide this advice.
5. Further, it needs to be made clearer to participants that they are not getting a diagnosis and while they are getting their test results, these are for research purposes. The Committee recommended the researchers have plans in place for having difficult conversations for the possibility of someone still ending up distressed if the results deviate from what they were hoping for, particularly in the case of antibody results at the start of the trial.
6. While it has been specified in some documentation, the Committee stated that the term “healthy” controls in all documentation is not addressed. Please ensure that if the controls are those without long-covid, the terminology used is adjusted and used consistently.
7. The Committee noted the references in the Data and Tissue Management Plan (DTMP) referring to historical/already collected samples. If these are being accessed for research, this needs to be explained and explicitly consented for.
8. The protocol, participant information and DTMP is vague when it comes to what data is being accessed, the purpose and what linking will take place. Please make this clear in the documentation what information you need for the research, when you are accessing it and how long it will be retained, etc.
9. The Committee queried if it was ethically sound to expect those identified as being in a higher risk category and unvaccinated to attend a lab visit under Level 3 conditions for the purpose of research. After discussion, the Committee concluded that it is best practice and more ethical for the study’s blood tests to only be performed under Level 2 Alert Level to minimise potential harms and would also help manage risks. The Committee acknowledged the perspective of urgency as these potential participants are hesitant to become vaccinated and may wait until after their involvement to get a vaccine. However, as this is observational research and there is no concrete certainty that their involvement in the study would provide participants assurance to their concerns about getting vaccinated, the Committee did not deem that this study needed to put participants in further risk. Please ensure it is clear that participants will be required to get these blood tests under Alert Level 2 or lower in their area in the participant information sheet.

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

1. Please review for typos, spelling, lay language and grammar.
2. The Committee noted specifically that there may be jargon or other words used that, while it is known to the Long-COVID community, it may not be known to the general population and the PIS should be fit for any lay person to understand.
3. The Committee stated the timeline/ruler used in the protocol would be helpful in outlining participation to potential participants. A flowchart about participation pathways would also aid in informed consent.
4. On page 3, please amend the following statement as it reads as firm rather than their choice “Some of the surveys may include sensitive questions that you feel uncomfortable answering. We encourage you to answer all the questions as we can learn better that way, but the decision is up to you.”
5. On page 6, please clarify what will happen if people do not consent for this portion “If you choose to withdraw, we will ask for your consent that you understand that the data and analysis performed up to the point when you withdraw may continue to be processed.”
6. Please advise potential participants that questionnaires are only submitted for data if it is completed and fully submitted.
7. Under risks, please provide the following: “Not much is known about why some people get long-covid and there is a small chance that vaccination of long-covid patients could potentially make their symptoms worse. If you have concerns, please discuss these with your GP or another health professional.”
8. CF includes no questions about whether participants wish to receive their own results. The PIS mentions that they will be asked to provide consent for this.
9. Please ensure the finger-prick option is provided to all participants but explain how this limits their participation.

**Decision**

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

1. Please address all outstanding issues raised by the Committee.
2. 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).*
3. Please update the data and tissue management plan to ensure the safety and integrity of participant data and tissue *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15, 14.16&14.17).*
4. 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.s17).*

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