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| **Committee:** | Northern B Health and Disability Ethics Committee |
| **Meeting date:** | 05 October 2021 |
| **Meeting venue:** | <https://mohnz.zoom.us/j/7894526927>  Meeting ID: 789 452 6927 |
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| **Time** | **Item of business** |
| 12.00pm | Welcome |
|  | Confirmation of minutes of meeting of 07 September 2021 |
| 12.20pm | **New applications** |
| 12.20-12.45pm  12.45-1.10pm  1.10-1.35pm  1.35-2.00pm  2.00-2.20pm  2.20-2.45pm  2.45-3.10pm  3.10-3.35pm  3.35-4.00pm | 21/STH/232 Kate / Gabrielle  2021 EXP 11163 Kate / Julie / Barry  2021 FULL 11027 Susan / Gabrielle  2021 FULL 11130 Maxine / Leesa  *Break (20 minutes)*  2021 FULL 11036 Kate / Julie / Barry  2021 FULL 10979 Susan / Gabrielle  2021 FULL 11242 Susan / Leesa  2021 EXP 10950 Maxine / Leesa |
| 4.00pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Mrs Kate O'Connor | Lay (ethical/moral reasoning) | 13/08/2021 | 16/08/2021 | Present |
| Mrs Leesa Russell | Non-lay (intervention studies), Non-lay (observational studies) | 13/08/2021 | 16/08/2024 | Present |
| Ms Susan Sherrard | Lay (consumer/community perspectives) | 19/03/2018 | 19/03/2022 | Present |
| Mr Barry Taylor | Non-lay (intervention studies), Non-lay (observational studies) | 13/08/2021 | 16/08/2024 | Present |
| Ms Maxine Shortland | Lay (consumer/community perspectives) | 13/08/2021 | 16/08/2024 | Present |
| Dr Gabrielle Jenkin | Non-lay (intervention studies),  Non-lay (observational studies) | 13/08/2021 | 16/08/2024 | Present |
| Ms Julie Jones (co-opted from Central HDEC) | Non-lay (intervention studies) | 22/05/2020 | 22/05/2022 | Present for items 2 and 5 |

## Welcome

The Chair opened the meeting at 12pm and welcomed Committee members.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

## Confirmation of previous minutes

The minutes of the meeting of 7 September 2021 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **21/STH/232** |
|  | Title: | Vericiguat Outcomes Study in HFrEF |
|  | Principal Investigator: | Prof. Richard William Troughton |
|  | Sponsor: |  |
|  | Clock Start Date: | 20 August 2021 |

Richard Troughton 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 main objective of this study is to evaluate the efficacy of vericiguat compared with placebo on reducing the risk of cardiovascular death or heart failure hospitalisation. The secondary objectives are to evaluate the efficacy of vericiguat compared with placebo on reducing the risk of cardiovascular death. This is a randomized, placebo-controlled, parallel-group, multi-site, double-blind, event-driven, phase 3 clinical outcome of the sGC stimulator, vericiguat, in adults with chronic heart failure with reduced ejection fraction (HFrEF).

### Summary of resolved ethical issues

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

1. The Committee asked if the medicine that someone with heart failure would need to continue to take for the rest of their lives. The researcher explained that most heart failure medications have a lifetime recommendation unless a new indication presents or a complication occurs, and that this medicine, if effective, will also be used for life.
2. The Committee asked about the patient reported outcomes which is being done on an electric device and being sent to the vendor in the United States, and how timely the notification to New Zealand researchers would be if a participant indicated issues with anxiety or depression during the study. The researcher explained that he Is not concerned for the safety of participants due to the existing relationship between participants and the researchers, enabling them to pick up any issues with participants in real time rather than waiting for the results of the questionnaires.
3. The Committee noted the reference to legal representatives consent in the protocol and reminded the researchers that this is legally not an option New Zealand.

### Summary of outstanding ethical issues

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

1. The Committee asked about the standard of care for this condition. The researcher explained that the standard of care for heart failure in this setting is complex where the pumping of the ventricle is reduced. The standard of care itself is a combination of a diuretic to get rid of excess fluid with a beta blocker. The Committee requested a broad outline of what standard of care entails is detailed the participant information sheet and consent form (PIS/CF).
2. The Committee asked if participants receiving benefit during the trial will be moved onto an open label extension. The researcher explained that while there is no open label component of the study currently, they intend to follow this up with the sponsor and make a case for an open label continuation. The Committee requested the PIS/CF is updated to clearly state whether or not study medication will be available after the study ends.
3. The Committee asked about the staggered enrolment approach which will stop when there have been 590 deaths which seems an unusual design to the Committee. The researcher explained that there has been a change to determining the stop date based on events that give power to demonstrate an effect, such as death, rather than an arbitrary time period. This change in design is to ensure the study is powered sufficiently to test the research hypothesis. The Committee advised that given the study duration is linked to the number of deaths that will occur, this should be more clearly and delicately explained to participants in the PIS/CF.
4. The Committee advised that the protocol did not sufficiently address the management of data and tissue. Pease supply a data and tissue management plan for the lifecycle of the study to ensure the safety and integrity of participant data and tissue that complies with *National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15a and 14.17.* Please use the [Data and Tissue Management Plan template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/hdec-data-tissue-management-template-oct2020.docx) available on the [HDEC website](https://ethics.health.govt.nz/guides-templates-and-forms/) and ensure the template is modified to appropriately reflect the data management requirements of this study.
5. The Committee noted the researchers confirmation that the sponsor and other parties will not be getting identifiable information. Please amend the PIS/CF accordingly.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF) in addition to those mentioned above:

1. Please make it clear who is sponsoring the trial and who is getting paid for the different sites. (The DHB not the individual doctor) in both PIS/CFs.
2. Please provide equitable reimbursement of costs for participants and amend paragraph 18 to state that specific expenses will be covered.
3. Please supply the full address of the lab.
4. Please amend the ‘If you become pregnant’ section to state that collecting data about their baby will only be done with additional consent.
5. Please add frequencies for the side effects.
6. Please ensure the ‘My Information’ section accurately distinguishes identifiable and coded data and details who has access to the data.
7. Please amend section 8 of the consent form to make it clear that the testing will be done with the participants consent, e.g. “by signing this consent form you agree to undertake this testing if the need arises”.

### Decision

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

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

After receipt of the information requested by the Committee, a final decision on the application will be made by Ms. Kate O'Connor and Dr Gabrielle Jenkin.

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| **2** | **Ethics ref:** | **2021 EXP 11163** |
|  | Title: | Standalone Stents as Second-Stage Surgery Study |
|  | Principal Investigator: | Dr Jesse Gale |
|  | Sponsor: |  |
|  | Clock Start Date: | 14 September 2021 |

Jesse Gale was present via videoconference for discussion of this application.

### Potential conflicts of interest

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

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

### Summary of Study

1. This intervention study aims to understand 1) In patients with both mild-moderate glaucoma and cataract, would it be more cost-effective to use iStent combined with cataract surgery, or delayed for use in those for whom it is still indicated after cataract surgery; 2) would standalone (i.e. not combined with cataract surgery) iStent use be considered cost-effective in pseudophakic eyes (eyes that have previously had cataract surgery); and 3) to assess the effectiveness of standalone iStent implantation in pseudophakic eyes.

### Summary of resolved ethical issues

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

1. The Committee asked about the lower rate of cataract/glaucoma in Māori and if it is a detection issue. The researcher explained that it is not a detection issue however there is not enough evidence to confidently say if Māori have a lower glaucoma rate.

### 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 peer review submitted did not use the HDEC template. (*National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.26.)* Please use the [Scientific Peer Review Template](https://ethics.health.govt.nz/guides-templates-and-forms/scientific-peer-review-submissions-guidance/) available on the HDEC website to address this.
2. The Committee asked about the submission of questionnaires for this study. The researcher explained that the questionnaire will be resubmitted to HDEC for review.
3. The Committee requested the data management section of the protocol (page 8) more accurately distinguishes between anonymised, deidentified and re-identifiable data.
4. The Committee advised that storing identifiable clinical data in a spreadsheet and on a laptop does not provide adequate security of data which should be stored on a secure server. Please consider using the DHB’s secure database (Redcap or Qualtrics) and update the Committee on the database used and how secure it is. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.11.)* Please also update section 6.3 accordingly.
5. The Committee requested more information about what cloud service the researchers will be using and its security. The Committee suggested using an option available from the DHB.
6. To satisfy the data management issues identified by the Committee, please use the [data management plan template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/data-only-management-template-oct2020.docx) from the HDEC website as a guide.
7. The Committed requested the protocol specifies what constitutes adverse events, how they will be categorised, recorded, managed, and what system (i.e. MEDRA) will be used. The Committee advised that Medsafe and CARM do not receive adverse events relating to research, only clinical practice. Please seek advice on how best to do this and respond to the Committee accordingly.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF) in addition to those mentioned above:

1. Please review the 'What happens to my information section' of [HDEC’s PIS/CF template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc) and incorporate relevant components into the PIS/CF. This section should align to the information in your data management plan. Please ensure the following issues are addressed;
   1. a better explanation of future research
   2. data risks of this study
   3. participant’s right to correct information
   4. participants right to withdraw from the study and what will happen to their data
   5. distinguish between identifiable and coded data and who has access.
   6. provide more detail about the participant’s right of access to information and withdraw information.
   7. participants data will be used internationally and how that data will anonymised
   8. publication of data with no identification of participants
   9. HDECs’ access to data for audit purposes.
2. Please ensure all consent form items have been explained in the body of the information sheet (e.g. provision of study results, notifying GP).
3. Please provide a reason for why you would need to contact the GP.
4. Please include an approval of the Ethics Committee statement section.
5. Please include a provision of compensation section.
6. Please include a ‘who to contact’ section.
7. Please include a ‘responsibilities’ section.
8. These sections that need to be added are all in the HDEC’s PIS/CF template linked above.

### Decision

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

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

After receipt of the information requested by the Committee, a final decision on the application will be made by Mr Barry Taylors and Ms Kate O'Connor.

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| **3** | **Ethics ref:** | **2021 FULL 11027** |
|  | Title: | EDP 938-201: A Study to Evaluate EDP 938 Regimens in Infants With RSV (RSVPEDs) |
|  | Principal Investigator: | Dr Thorsten Stanley |
|  | Sponsor: |  |
|  | Clock Start Date: | 16 September 2021 |

Marina Dzhelali and Thorsten Stanley was present via videoconference for discussion of this application.

### Potential conflicts of interest

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

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

### Summary of Study

1. This intervention study EDP-938 is being developed as a potential treatment for respiratory syncytial virus (RSV) infection. RSV is the leading cause of lower respiratory tract infection and presents a significant health challenge in small children. To address the unmet medical need for a safe and effective RSV therapy this study is being conducted to investigate EDP-938 in infants and children (aged 28 days to 36 months) as a potential treatment for RSV infection.

### Summary of resolved ethical issues

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

1. The Committee noted the vulnerable young age of the population and queried why this study is not being done with healthy and/or older children first. The researcher explained that as it is treating a virus it cannot ethically be tested on healthy children. She further explained that RSV normally presents in children under three years of age and therefore using older children is not feasible.
2. The Committee noted that the insurance cover starts on the 1 December and asked for confirmation that the study will not start prior to this. The researchers explained that they wish to start on the on 1 December, however this start date may be delayed due to COVID-19 lockdowns. Under the current insurance only 2 participants in New Zealand can be enrolled.
3. The Committee noted the application questions on the risks and benefits to Māori (C4 and C5) were not answered and should have been carefully considered for a study like this. Likewise the response to Pasifika cultural issues was not what the Committee would expect. Please be mindful of this for future applications.
4. The Committee asked about how the Māori consultation process is progressing. The researchers confirmed that they have submitted the study for Māori consultation and confirmed this process will be completed before their study begins.
5. The Committee noted the researchers confirmation that only two participants will be enrolled in New Zealand. It advised that if the study were to recruit more than two participants, the researchers will need to ensure there is adequate insurance and submit an updated insurance certificate.
6. The Committee noted the advertising material does not state that the study is comparing against placebo. It advised that none of the submitted advertising is approved for use in New Zealand.

### Summary of outstanding ethical issues

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

* + Please include a bolded warning on the first page that this is the first time this drug has been given to children.
  + Please amend wording of the following statement, “Your child will also be asked to complete some procedures” as the child will not be asked.
  + Please amend all wording of “subjects” to “participants”.
  + Please amend all wording of “race” to “ethnicity”.
  + Please add the approximate time it takes to fill in the e-diary.
  + Please consider mentioning breastfeeding mothers earlier in the document.
  + Please replace side effect percentages with chance of occurrence (e.g. 1 in 10).
  + Please amend “Suffers” to “Experiences” on page 12.
  + Please amend “Required to do something” to “Asking to do something”.
  + Please add contact details for the Māori health support.

**Decision**

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

* Please address all outstanding ethical issues raised by the Committee.
* Please update the participant information sheet and consent form, taking into account 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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| **4** | **Ethics ref:** | **2021 FULL 11130** |
|  | Title: | PRP versus corticosteroid RCT |
|  | Principal Investigator: | Dr Jordan Davis |
|  | Sponsor: |  |
|  | Clock Start Date: | 16 September 2021 |

Jordan Davis, Cathy Sorensen and Catherine Bacon were present via videoconference for discussion of this application.

### Potential conflicts of interest

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

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

### Summary of Study

1. The study investigates patient-reported outcomes following platelet-rich plasma (PRP) compared to corticosteroid injection (CSI) for treatment of adhesive capsulitis (frozen shoulder). A randomised controlled trial.

### Summary of resolved ethical issues

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

1. The Committee queried what the cost implications will be for participants given that the standard care (steroid shots) would generally be covered by ACC. The researcher confirmed that PRP is not covered by ACC and costs approximately $400 per injection which the patient would pay for. He confirmed that further PRP treatment may be required (i.e. up to 3 injections over 6 weeks) but that they have seen patients respond well to a single shot.
2. The Committee queried how the safety of participants will be maintained if clinicians are blinded. The researcher confirmed that the techniques for providing the shot and taking blood are the same for both study arms.

### Summary of outstanding ethical issues

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

1. The Committee noted that the researchers appear to be using identifiable data (e.g. accessing medical records) and that their answer to application question S6 should have been yes.
2. The Committee advised that questions E6.1 and E7 require the description of your data and safety management, not your adverse event collection. Further, it is not clear from the protocol what previous phasing of the therapy has occurred and what evidence of safety that exists. The Committee advised that a safety monitoring plan is required and a data and safety monitoring committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.25 – 11.40).* Please also outline in your protocol, literature reviews that document the safety data from previous trials that have occurred using this therapy.
3. The Committee advised of the dual-role conflict that exists when researchers are both the study investigator and treating clinician. It requested more information on how the researchers plan to manage the ethical challenges associated with dual roles such as undue influence, compromising the voluntary nature of participation, informed consent and privacy, ensuring separation of roles. (*National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.23 – 11.24).*
4. The Committee stated that it is not clear if the information being inputted into the orthosports database will be accessed by others outside the researcher team. The Committee advised that research data is distinct from standard clinical data and these records should be kept separate and accessed by authorised personnel only (i.e. research staff). Further, it would be acceptable to share relevant information (e.g. participant outcomes) to the participant’s treating clinician, however this needs to be explained and consented to by participants. Please reconsider and advise how you plan to manage these concerns raised by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.08 – 12.15).*
5. The Committee requested that the orthosports research database mentioned in application (G1) is explained in the data and tissue management plan (DTMP).
6. The Committee advised that the DTMP is incomplete, and the template needs to be modified to appropriately reflect the data management requirements of this study. (*National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15a and 14.17).* The Committee requested the following changes;
   1. please remove the template text and fill in the information requested (i.e. where there is a red line).
   2. please detail the security arrangements in use for the Socrates Orthopaedic Outcomes Software system and that the company will not have access to the participants’ results
   3. please add laboratory information to Section 2 for the 'blood counts' under New Zealand laboratories
   4. data is being stored on Medtech which is a standard clinical records database and is also an identifiable system. Please clarify how the research information will be recorded, de-identified, and managed separately (as per the Committee’s earlier point)
   5. please remove section 8.5 as there will be no future unspecified research.
7. The Committee advised that contrary to the answer in the application (c3.3), this study design is not kaupapa Māori.
8. The Committee noted that the application stated there will not be advertising but mentions emailing other clinics to refer patients. The Committee requested the referral email is provided to HDECs for review.
9. The Committee notes that the questionnaires ask about anxiety and depression and advises that researchers have a duty to arrange support for participants should their answers indicate they are at risk of mental health issues. This includes a procedure to review forms that may suggest distress or mental health concerns before analysis and close to the time the forms are completed. Please provide a safety plan addressing the concerns raised by the Committee *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.25 and 11.47).*
10. The Committee advised that a sponsor, an organisation that is responsible for the conduct of the research, must be identified for this study and you cannot operate without one (H5). Please update the study documentation.
11. The Committee requested that for future applications the study documentation is submitted as clean copies with tracked changes and comments removed. Tracked changes are only required for post-approval amendments.
12. The Committee advised that information provided on the expert peer review is incomplete as preference is for reviews to be done by senior colleagues (e.g. consultants or head of department) rather than registrars. Further, the Committee needs to see how the researchers have incorporated the feedback of reviewers or the rationale for not incorporating it. (*National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.26.*). Please advise how the feedback of Jeremy Steinberg has been incorporated into the study design.
13. The Committee stated that it is unclear in the application and protocol which private organisation the research is being undertaken in (i.e. orthosports vs AUT Millennium) and where the responsibility for the study lies. Please clarify this and the relationship between the organisations and update the protocol.
14. The Committee advised that the information in application question F5, needs to be outlined in the protocol including how the researchers will ensure study number is matched back to participant and their blood to ensure that PRP is not accidentally given back to the wrong person. The DTMP suggests this will be kept identifiable. Please add this to your study procedures in your protocol.
15. The Committee requested the protocol includes the names of the sites being used in the study (e.g. laboratories and interview locations, etc.).
16. The Committee stated that in the method section within the calibration section of the protocol, it is unclear where samples for each test will be sent. Please clarify this in the protocol.
17. The Committee advised that the consent process should occur before significant screening occurs (i.e. methods section). Please adjust these process steps in the protocol.
18. The Committee advised that the patient complaint process outlined is incorrect as ethical issues have been described and not a process to manage complaints. Please amend the protocol accordingly.
19. The Committee requested the stopping rules identified in application question E8 are formalised in the protocol.
20. The Committee requested the protocol specifies exactly what information is being collected from the participants’ medical records and how it will be used.
21. The Committee recommended reviewing the protocol to ensure it has all the features required under *National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.8.* In particular the review of existing literature and justification for study design, ethical issues and plan for management, termination rules and an adverse events process including a data monitoring committee (with list of members).

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

1. Please remove the parent/guardian panel from the consent form as this is not needed if only enrolling adults.
2. Please consider using lay language in the documents (e.g. replace ‘adhesive capsulitis’ with ‘frozen shoulder’).
3. Please rewrite the ‘Purpose of study’ section to simplify it and explain that it is essentially a drug comparison. Also, please move the information about publishing, confidentiality, etc. to elsewhere in the document.
4. Please rewrite the ‘Who can take part’ section to address who is eligible and include some broad information about inclusion/exclusion criteria.
5. With regards to the information about the injection process, please be more specific about what medical information and clinical records are being used (e.g. ‘We will use information about your injection process, your medical conditions relating to the surgery’, etc.). Please also explain what ‘pertinent’ medical information is.
6. In the ‘Risks and benefits’ section, please provide evidence-based information about the risks including the likelihood as a ratio (e.g.1:10 participants have xtz.). For guidance, please refer to *National Ethical Standards for Health and Disability Research and Quality Improvement, Table 7-1* for the key elements.
7. Please also discuss the risk of accidentally receiving someone else's PRP and what processes are in place to ensure this will not occur.
8. Please add withdrawal information and explain rights to withdrawal to the ‘Change my mind’ section. Please use the standard wording in the HDEC’s [PIS/CF template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc).
9. Please add standard ACC statement. Refer to the HDEC’s [PIS/CF template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc). Also, please explain the normal situation regarding ACC funding for the Standard of Care treatment, and what costs participants might occur if further injections of either arm are indicated.
10. Please remove the yes/no tick boxes from the consent form for items that are not truly optional.
11. Please be very clear what the PRP process entails under the study procedures, and if participants are to not use other drugs during the trial duration (e.g. anti-inflammatory) and what they should do if they experience pain and how that will be managed.
12. Please also be clear that participants may get a treatment that is not the usual treatment and that it is not known if it is effective, which is why this research is being undertaken. (E.g. ‘…there have been studies already done that showed that PRP may be effective...)

### Decision

This application was *declined* by consensus, as the Committee did not consider that the study would meet the ethical standards referenced above. The Committee recommended the researcher re-apply to the NTB HDEC as it has reviewed this initial application and will have more context for the re-application.

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| **5** | **Ethics ref:** | **2021 FULL 11036** |
|  | Title: | The Cost of MND in New Zealand |
|  | Principal Investigator: | Dr Alan Stanley |
|  | Sponsor: |  |
|  | Clock Start Date: | 17 September 2021 |

Tony O’Connor 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 aims to estimate from a societal perspective (government and individual) the 1-year direct health care and indirect productivity loss, including informal care cost, of Motor Neurone Disease (MND) per capita in New Zealand in 2021.

### Summary of resolved ethical issues

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

1. The Committee noted the digital survey and consent form and queried equity of access for those who do not have access to a computer or the Internet. The researcher advised that the MND community are largely members of MND NZ and communications with this group are mostly online.
2. The Committee noted the researcher’s confirmation that the data will be stored at MND New Zealand in anonymised and deidentified form.

### Summary of outstanding ethical issues

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

1. The Committee noted the broad approach to recruitment, through the MND Registry, support workers, neurologists, and Facebook adverts and the potential for participants to receive multiple survey invitations. It was concerned that multiple invitations may be perceived as pressure to participate; particularly if they are being referred by their neurologist. The Committee suggested building in an option for people to decline further invitations and removing the neurologist referral pathway.
2. The Committee noted the researcher’s confirmation that some of the MND community will have diminished capacity to consent and his intention to enrol participant through proxy-consent. It advised that proxy-consent for adults is limited in New Zealand and participants can only be enrolled into research if [Right 7(4) of the Code of Health and Disability Services Consumers’ Rights](https://www.hdc.org.nz/your-rights/about-the-code/code-of-health-and-disability-services-consumers-rights/) is satisfied which it would not be in this situation. The Committee advised that the supported decision-making model would be acceptable for those who could give informed consent with assistance *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 6.6 – 6.12).* However, those who cannot provide informed consent for themselves will need to be excluded from the study. Please provide an updated protocol detailing the revised enrolment/consenting processes and the amended inclusion/exclusion criteria.
3. The Committee added that caregivers and family members can consent to giving information about their own experiences, but they cannot consent to provide information about the potential participant without their fully informed consent.
4. The Committee advised that should the researcher discover at the end of this study that the population group that is unable to consent is an important group to survey, he could apply to HDECs with a follow up survey addressing the requirements for enrolling participants into research without consent. Please refer to *National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.50 – 7.71)* for guidance*.*
5. The Committee noted that the anonymous survey respondents will not be able to enter into the prize draw without agreeing to the data linking. The Committee requested a solution for this and suggested a thank you page at end of the survey with an option to click through to a separate form/survey where they can provide their contact details for the prize draw.
6. The Committee advised that the language used in the Facebook adverts (i.e. "ground-breaking, peer-reviewed research") is overstated. Please update the advertisements, using less dramatized language. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.10).*
7. The Committee advises that the document provided is not adequate evidence of peer review. Please supply an independent peer review that complies with *National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.26.* Please use the [Scientific Peer Review Template](https://ethics.health.govt.nz/guides-templates-and-forms/scientific-peer-review-submissions-guidance/) available on the HDEC website to address this.
8. The Committee advised the process for getting in touch with the research team to ask questions is too onerous for participants. Please add a contact phone number to the email, PIS/CF, and MND website.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF) in addition to those mentioned above:

1. Please include a header with logos, addresses of sponsor, contacts, friendly greeting, and footer, etc in the PDF version. Please provide this version (as a participant would view it online) to HDECs.
2. Please review the 'What happens to my information section' of [HDEC’s PIS/CF template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc) and incorporate relevant components into the PIS/CF. This section should align to the information in your data management plan. Please ensure issues such as the risk of data / confidentiality breach, access to identifiable and de-identified data (and distinguishing between de-identified and anonymous data), data-linking and future uses of data are addressed.
3. Please make it clearer that only the principal investigator will have access to identifiable information, and that when it is stored at the MDN registry it will not be identifiable.
4. Please include options for withdrawal and withdrawal of data for those that provide identifiable information and add some timeframes (e.g. 6 months).
5. The form is heavily weighted towards participants agreeing to the data linkage and the increased risks of this need to be more clearly explained
6. Please replace ‘will’ with ‘may’ in the following statement, ‘The study’s findings will help MND New Zealand advocate for the needs of people living with MND.’
7. Please remove reference to consent as ‘conditions’ as this is not a contract but rather participants are being asked if they understand their responsibilities and are willing to participate.
8. Please ensure items mentioned in the consent form have been introduced and explained in the body of the information sheet first (e.g. data linking).
9. Please more clearly define the difference between the two options (with and without data linking) and explain the risks and benefits of each. As above, please explain this earlier in the information sheet prior to the consent form.
10. Please standardise the terms used so that participants do not think you are referring to two different things (i.e. use questionnaire or survey).
11. Please add information about HDEC audits and potential legal reporting requirements to the body of the information sheet and add a consent item. For guidance on wording, please see the [HDEC’s PIS/CF template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc).
12. Please add the Māori support contact details.
13. Please add the funding organisation.
14. Please better distinguish between MND approval of the study and HDECs approval of the ethical aspects of the study.
15. Please add the following consent item, ‘I have had the opportunity to use a legal representative, whanau/ family support or a friend to help me ask questions and understand the study.’
16. Please add ‘I understand my information may be sent overseas’ to the following consent statement; ‘I agree to my anonymised information being used for future research related to Motor Neurone Disease and/or for other medical and/or scientific research that is unrelated to the current study’.
17. Please be mindful of the language used so that participants are not framed as a burden. For example, ‘this study will look at the money lost to society due to people with MND…’

### Decision

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

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

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

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| **6** | **Ethics ref:** | **2021 FULL 10979** |
|  | Title: | MK-1654-007: RSV Palivizumab-Controlled Evaluation of Safety, Efficacy, and Pharmacokinetics of MK-1654 in Infants and Children at Increased Risk for Severe RSV Disease |
|  | Principal Investigator: | Dr Michael Meyer |
|  | Sponsor: |  |
|  | Clock Start Date: | 17 September 2021 |

The principal investigator was not present for discussion of this application.

### Potential conflicts of interest

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

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

### Summary of Study

1. The study is a phase 3, multicentre, randomized, partially blinded, palivizumab-controlled study to evaluate the safety, efficacy, and pharmacokinetics of MK-1654 in infants and children at increased risk of severe respiratory syncytial virus (RSV) disease. 15 New Zealand participants of a total of 1000.

### Summary of outstanding ethical issues

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

1. The Committee noted that this study group includes extremely unwell infants and children and the intention to recruit participants as soon as possible after birth. Given this, the Committee requested clarity on how the enrolment process will be managed to mitigate further distress to parents and provide them enough time to consider involvement in the study. (*National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.4, 7.7 – 7.8).*
2. The Committee requested clarification on why potential participants with Downs Syndrome condition are targeted for the second phase of the study. (*National Ethical Standards for Health and Disability Research and Quality Improvement, para 6.2).*
3. The Committee were concerned that the number of study visits which include 3 days after birth may be overly burdensome for parents. *National Ethical Standards for Health and Disability Research and Quality Improvement, para 8.3.*
4. The Committee noted childcare costs will be reimbursed and requested clarification on how this will work and how consistency of reimbursement between the two sites will be maintained. (*National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.8).*
5. The Committee requested more information about the dosing protocol for children on the ECMO sub-study as the study documentation states only that it is at the discretion of the principal investigator. In particular, the number of additional doses participants will receive and when, and why dosing is at the discretion of the principal investigator. *National Ethical Standards for Health and Disability Research and Quality Improvement, 7.15 and Table 7-1*.
6. The Committee advised that the data and tissue management plan (DTMP) provided has not been customised to the study sufficiently and therefore making it difficult to determine what is happening with the data. Please modify the DTMP to appropriately reflect the data management requirements of this study, paying particular attention to distinguishing between anonymised and deidentified tissue. *National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15a and 14.17.*
7. The Committee was unclear why rectal temperature taking is necessary given it is stressful to infants and families who are already vulnerable. It queried if other options could be made available such as armpit testing or forehead testing (i.e. Temporal Artery thermometry). *National Ethical Standards for Health and Disability Research and Quality Improvement, para 8.3.*

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

1. Please provide a lay title.
2. Please replace the phrase ‘like tossing a coin’ (page 4).
3. Please make it clear earlier in the document (on page 4) that in Season 1, parents will not know which drug their child is getting.
4. Please add macrons to ‘whānau’ (page 11).
5. Please include examples of information collected in diary (page 12).
6. Please change date at bottom of page so it does not run together (page 12).
7. Please change 'required' to ‘asked’ (page 21).
8. Please add Māori support contact details (page 21)
9. The offer of an interpreter at the end of the document is not practical. Please move to front of document (page 22).
10. Please clarify when the RSV season/s are.

FBR PIS/CF

1. Please add ‘your child’ to ‘We may also use your sample...’ (page 2).
2. Please provide Māori support contact details (page 7).
3. The offer of an interpreter at the end of the document is not practical. Please move to front of document (page 7).

### Decision

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

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| **7** | **Ethics ref:** | **2021 FULL 11242** |
|  | Title: | ATB1651-101: A Study to Assess ATB1651 in Adults with Mild to Moderate Onychomycosis |
|  | Principal Investigator: | Dr Chris Wynne |
|  | Sponsor: |  |
|  | Clock Start Date: | 20 September 2021 |

Chris Wynne and Courtney Rowse were present via videoconference for discussion of this application.

### Potential conflicts of interest

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

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

### Summary of Study

1. The study aims to assess the safety, tolerability and Pharmacokinetics of ATB1651 (antifungal agent) in adults with mild to moderate onychomycosis (a contagious fungal infection of the toenails). A phase 1, first-in-human, randomized, double-blind, placebo-controlled multiple ascending dose study with approximately 48 New Zealand participants.

### Summary of resolved ethical issues

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

1. The Committee noted that application question B1 has been incorrectly answered and should be yes, as the study is a treatment that holds the prospect of direct benefit for individual participants.
2. The Committee disagreed that there is no standard of care for this condition as stated in the application. The Committee has seen previous studies in the condition and although there is not one standard of care that is well-described, they do exist for this condition.
3. The Committee noted the reference to legal representatives consent in the protocol (page 65) and New Zealand and the researchers confirmed that they understand this is not an option in New Zealand.

### 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 researchers confirmation participants’ privacy will be protected by ensuring the photographs have any identifying or revealing marks removed. Please update the participant information sheet and consent form (PIS/CF) with this information to reassure participants.
2. The Committee noted there is a pain scale and queried what process will occur if participants report increasing or extreme pain. The researcher clarified that the study medication would be stopped, the participant would exit the study and referred to their GP for ongoing medical care. The Committee requested this is added as a breakthrough medication clause to study documentation.
3. The Committee noted the researchers clarification that the nail notch is a painless procedure involving a small scratch to the nail in order to get a micro biologic sample. Please include this as a study procedure and in the risks/benefits section of the PIS/CF.
4. The Committee informed the researcher that it is not acceptable to stop a therapeutic study for administrative or commercial reasons. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.37).* Please amend the study documentation accordingly.
5. The Committee queried why the use of paracetamol during the course of the study is at the discretion of the principal investigator (PI). The researcher clarified that low doses can be used by participants without permission but anything higher may affect PK analysis and therefore needs the PI to review. He added however, that this restriction does not apply to emergency situations. The Committee asked that participants are well informed of this.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF) in addition to those mentioned above:

1. Please include a lay title (i.e. fungal toenail infection).

PIS/CF Part A

1. Please supply the full addresses for all laboratories in the PIS/CF Part A.

PIS/CF Part B

1. Please state how long participants are required to self-administer the medication at home in the PIS/CF Part B.
2. Please provide more detail on when and why the fasting is required (page 7).
3. Please state that the treatment will not be available after the study finishes (page 15).

### Decision

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

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

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| **8** | **Ethics ref:** | **2021 EXP 10950** |
|  | Title: | The Early & Intensive SCI-MT Trial |
|  | Principal Investigator: | Dr Joanne Nunnerley |
|  | Sponsor: |  |
|  | Clock Start Date: | 20 September 2021 |

Joanne Nunnerley and Lisa Harvey were present via videoconference for discussion of this application.

### Potential conflicts of interest

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

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

### Summary of Study

1. The study aims to determine whether people with recent spinal cord injury benefit from a 10-week program in which they receive an additional 12 hours a week of a particular type of physiotherapy called motor training. Motor training involves various exercises such as the practice of standing, walking or using the hands. We want to find out if this type of therapy increases strength and function if provided in a high dosage as part of initial rehabilitation after spinal cord injury.

### 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 how equipoise will be maintained when the control arm participants could choose to do more self-therapy if they feel they are missing out on what may be beneficial for them. The researcher clarified that the study therapy will be done after hours and potentially at a different gym to mitigate any real or perceived lack of treatment. The researchers added, that while they cannot stop the control arm participants doing more self-therapy, the intervention is about assistance from the trained therapist.
2. The Committee queried if the unit has adequate resources to cover the extra therapy and ensure that non-participants are not missing out on their regular care. The researchers clarified that the therapy will be undertaken outside of regular treatment hours and therapists will be paid overtime to ensure the study does not impact regular treatment.
3. The Committee advised that the answer to question C15 should have been yes, as the Māori consultation letter supplied suggests that the study could have health benefits for Māori which may reduce inequity.
4. The Committee queried how researchers plan to keep participants blinded when there will be an observer present in the gym. The researcher advised that health and safety requires two additional people to the participant present at all times which will help obscure the real purpose of the observer. The researcher added that they may not be able to keep the observing blinded to all participants, it is being used for fidelity reasons and is not a critical aspect of the trial.
5. The Committee noted the researcher’s confirmation that there are no mental health questions in the survey.

### 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 were concerned with the conflict of interest that presents when members of the participants standard clinical care team are recruiting and administering the intervention. The Committee advised that participants may feel pressure to take part in the study due to the clinician-patient relationship and that a greater deal of distance needs to be created to mitigate this (e.g. participants consented by someone external to the clinical team). Please revise the recruitment process to ensure that the required independence is built in to mitigate this conflict. (*National Ethical Standards for Health and Disability Research and Quality Improvement, para* *11.23 – 11.24).*
2. The Committee was concerned that there is not adequate time between presentation of information and consenting for participants to fully consider the risks and benefits of the study. Please ensure there is time for potential participants to settle into the clinic after arrival (e.g. 48 hours) before approaching them about the study. Please also ensure participants are given enough time to consult with family and properly consider their involvement in the study once the study information has been presented to them (e.g. at least 3-4 days). (*National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.4).*
3. The Committee recommended evidencing support of the study from consumer groups as this adds credibility to the research.
4. The Committee advised involvement in research should not be stated as a health benefit for Māori as equal access to participate for Māori is the default expectation. Given Māori has a higher population representation for SCIs, the benefit to Māori question (C4) needs to be reconsidered (i.e. how you will help Māori to participant in this research). In addition, the Committee recommended the researcher is mindful of this for any future applications.
5. The Committee requested cultural issues for Māori and Pacifica are carefully considered for this study (C5).
6. The Committee requested more information on the observation process, such as the type of data the observer will be collecting, the scale or audit criteria used to evaluate the process, and the training process to ensure consistency of observation. Please update the protocol accordingly.
7. The Committee advised that it is difficult to assure confidentiality of a focus group and it is not the same as an interview with a researcher. While confidentiality can be requested from the focus group, you cannot stop them from revealing information. Please amend the study documentation accordingly.
8. The Committee advised that in New Zealand 16–17-year-olds can consent for themselves and do not need parental consent. Please ensure you do not enrol anyone into this study who may not consent for themselves. (*National Ethical Standards for Health and Disability Research and Quality Improvement, para 6.24).*
9. The Committee noted the researchers’ confirmation that there is a total of 220 participants and requested this is added to the protocol.
10. The Committee advised that it is not clear in the protocol that optional interviews are happening with participants up to two years later, only with key stakeholders. Please provide more information on the optional interview including an interview schedule for the Committee to review.
11. The Committee advised that emailing the scanned forms to Sydney is not secure enough for health data and requested this approach is reconsidered. It advised that it would accept password protected email if this is the only option, however best practice is to encrypt the email which could be done by the DHB using Citrix share file.
12. The Committee requests the HDEC’s [Data Management Plan template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/data-only-management-template-oct2020.docx) is reviewed and missing sections are incorporated into the data management plan provided (as an addendum if necessary). This includes what formats data will be collected in, who will be able to review these types of data, and future use of data. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15a.)*
13. The Committee requested clarification on who is transcribing the interviews and confirmation that they will sign a confidentiality agreement if external to the research team.
14. The Committee advised that information provided on the expert peer review is incomplete as HDECs need to see how the researchers have responded to the feedback (i.e. what has been incorporated into the study design or the rationale for not incorporating it). (*National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.26.*).
15. The Committee advised that it is not unnecessary to have a pregnancy notification form for this trial as there is no investigational product and therefore is unnecessary data collection. As participants are not informed of this collection, it may be perceived as a breach of privacy. The researcher agreed and will remove this.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF) in addition to those mentioned above:

1. Please proofread the PIS/CFs to correct typos and grammatical errors.

PIS/CF Participants

1. Please explain autonomic dysreflexia in lay language.
2. Pease add risks such as burnout or fatigue.
3. Please add risks associated with electrical stimulation therapy and the likelihood of them occurring (e.g. 1 in 20 chance of burns).
4. Please make it clear that the therapy will be undertaken after hours (i.e. weeknights and weekends) rather than stating it may be and is at the discretion of the principal investigators.
5. Please state the difficulties more clearly (e.g. therapy is an extra 12 hours, that is double what they would normally do and therefore they may find this physically or mentally challenging, etc).

PIS/CF Stakeholders

1. Please update the risk section regarding confidentiality for focus groups.
2. Please review for, and amend, copy and paste errors (e.g. If they withdraw, they will not receive usual care and rehab).
3. Please reduce the 2-3 pages of information management and confidentiality as this is excessive for interviews and focus groups.

### Decision

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

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

After receipt of the information requested by the Committee, a final decision on the application will be made by Mrs Leesa Russell and Ms Maxine Shortland.

## General business

1. The Committee noted the content of the ‘noting section’ of the agenda.
2. The Chair reminded the Committee of the date and time of its next scheduled meeting:

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| --- | --- |
| **Meeting date:** | 02 November 2021 |
| **Zoom details:** | TBC |

1. **Review of Last Minutes**

The minutes of the previous meeting were agreed and signed by the Chair and Co-ordinator as a true record.

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

The meeting closed at 4.20pm.