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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 18 June 2024 |
| **Zoom details:** | 965 0758 9841 |

| **Time** | **Review Reference** | **Project Title** | **Coordinating Investigator** | **Lead Reviewers** |
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| 12:30 - 1:00pm | 2024 FULL 19738 | Study of Paediatric Appendicitis Scores and Management Strategies | Ms Catherine Garvey & Dr Andrea Forde | Professor Stuart Dalziel |
| 1:00 - 1:30pm | 2024 FULL 20016 | Does iodine deficiency cause congenital hypothyroidism in preterm babies? | Dr Maree Kirk & Dr Sotera Catapang | Dr Benjamin Albert |
| 1:30 - 2:00pm | 2024 FULL 18953 | A 3D printed AFO for personalised form and function in patients with movement disorders | Mr Jonathan Darby & Dr Andrea Forde | Dr Julie Choisne |
| 2:00 - 2:30pm |  | Break 30 minutes |  |  |
| 2:30 - 3:00pm | 2024 FULL 19567 | A Phase 2b, Double-Blind, Randomized Extension Study to Evaluate the Long-Term Safety and Efficacy of PTC518 in Participants with | Dr Maree Kirk & Mr Derek Chang | Professor Tim Anderson (not attending) |
| 3:00 - 3:30pm | 2024 FULL 20202 | Huntington’s Disease | Mr Jonathan Darby & Ms Jade Scott | Dr Alexandra Cole |
| 3:30- 4:00pm | 2024 FULL 20183 | A Sequential, Randomized, Double-Blind, Placebo-Controlled, Phase 1 Single and Multiple Ascending Dose Study of LTG-305 | Ms Catherine Garvey & Dr Sotera Catapang | Dr Andrew Holden |
| 4:00- 4:15pm |  | Break 15 Minutes |  |  |
| 4:15- 4:45pm | 2024 FULL 20371 | A Phase 1b Study to Evaluate the Safety, Pharmacokinetics, Pharmacodynamics, and Efficacy of Cavrotolimod Alone and in  Combinations in Subjects with Chronic Hepatitis B Infection. | Mr Jonathan Darby & Ms Jade Scott | Professor Edward Gane |
| 4:45- 5:15pm | 2024 FULL 20396 | Open label dose escalation study to evaluate safety, tolerability, pharmacokinetics, and pharmacodynamics of repeated daily oral dosing of YCT-529 for 28 days in healthy men. | Dr Maree Kirk & Mr Derek Chang | Dr Rohit Katial |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Mr Derek Chang | Non-lay (Intervention studies) | 08/07/2022 | 08/07/2025 | Apologies |
| Dr Kate Parker | Non-lay (Observational studies) | 11/02/2020 | 11/02/2023 | Present |
| Dr Andrea Forde | Non-lay (Intervention studies) | 22/12/2021 | 22/12/2024 | Apologies |
| Ms Catherine Garvey | Lay (the Law) (Chair) | 19/03/2019 | 19/03/2022 | Present |
| Dr Sotera Catapang | Non-lay (Observational studies) | 11/02/2020 | 11/02/2023 | Present |
| Mr Jonathan Darby | Lay (the Law/Ethical and Moral reasoning) | 13/08/2021 | 13/08/2024 | Present |
| Ms Jade Scott | Non-lay (Intervention/Observational studies) | 15/08/2021 | 15/08/2024 | Present |
| Dr Maree Kirk | Lay (Consumer/Community perspectives) | 03/07/2023 | 02/07/2026 | Present |

## Welcome

The Chair opened the meeting at 11pm and welcomed Committee members, noting that apologies had been received from Dr Kate Parker.  
  
The Chair noted that it would be necessary to co-opt members of other HDECs in accordance with the Standard Operating Procedures. Dr Maree Kirk confirmed their eligibility and were co-opted by the Chair as members of the Committee for the duration of the meeting.

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 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **2024 FULL 19738** |
|  | Title: | Study of Paediatric Appendicitis Scores and Management Strategies |
|  | Principal Investigator: | Professor Stuart Dalziel |
|  | Sponsor: |  |
|  | Clock Start Date: | 6 June 2024 |

Dr Stuart Dalziel 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 resolved ethical issues

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

1. The Committee clarified the statistician blinding of the patients in an attempt to remove bias. The clinicians would also be blinded, and all study-related forms filled in prior to the analysis to also help ensure blinding.

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 that the protocol was Australian-based and there needs to be a New Zealand specific appendix.
2. The Committee requested that the researcher provide a New Zealand specific Data Management Plan.
3. All researchers should collect good quality ethnicity data unless there is a particular justification for not doing so. Ethnicity data for New Zealand sites is provided to HDEC at the time of the final report; please collect at a site level if not required for the protocol *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.20)*.
4. The Committee need scientific expert peer review to display this is scientifically valid and should be done after amendments to protocol have been made. The Committee recommended use of the [template available](https://ethics.health.govt.nz/guides-templates-and-forms/scientific-peer-review-submissions-guidance/) on the HDEC website.
5. The Committee requested a clear process for ensuring that the verbal consent was being documented as it was given. This should be included in the protocol.
6. The Committee queried the justification of the pregnancy exclusion and how the pregnancy tests and diagnosis would be managed. The researcher clarified that concealed pregnancy is rare in this cohort and that if this occurs the person would not be included in the study and the pregnancy would likely be found via urinalysis prior to the study. The researcher also noted that should anyone come into the hospital with abdominal pain that a concealed pregnancy (including pregnancy testing) would be managed through Standard of Care. Please include this in the protocol.
7. The Committee requested clarification as to how the distress of participants will be managed given that informed consent is being sought from participants in an Emergency Department setting.
8. The Committee suggested that the assent form be simplified, and the language reviewed to be easier to read. The Committee suggested that the researchers test the forms in the age-group prior to being used.

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

1. Please detail where data will be sent overseas.
2. Please remove all references that are Australian-specific and replace with New Zealand references where necessary.

**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).
4. 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).
5. Please supply a more detailed data management plan to ensure the safety and integrity of participant data. This can be a standalone document or incorporated as part of the protocol *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15a).*

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

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| **2** | **Ethics ref:** | **2024 FULL 20016** |
|  | Title: | Does iodine deficiency cause congenital hypothyroidism in preterm babies? |
|  | Principal Investigator: | Dr Benjamin Albert |
|  | Sponsor: |  |
|  | Clock Start Date: | 6 June 2024 |

Dr Ben Albert and Dr Ashleigh Brown 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 resolved ethical issues

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

1. The researcher clarified that twins may be enrolled and this would be done through determination of elevated hormone levels and one twin would be used as the other’s control (likely scenario). The researcher noted that a large number of twins would be in this pre-term group and eligible to participate in the study.
2. The Committee queried if there would be any weighted recruitment to ethnicities identified as being of higher risk groups such as Māori and Pasifika groups. The researcher explained that it would be likely that these groups would already be sufficiently sampled due to the incidence in the group with hypothyroidism. The researcher noted that it would be harder to ensure matched controls from these groups. They clarified that this would be assessed at 2/3rds total recruitment.
3. The Committee clarified that the selected funding grant did not provide peer review hence alternative peer review was uploaded.
4. The Committee clarified that the pre-natal records would not be included in this study.
5. The Committee clarified the scheduling for the breast-milk testing.

Summary of outstanding ethical issues

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

1. The Committee requested that references be included in all points including those described as “unpublished” in the protocol.
2. The Committee noted that all researchers should collect good quality ethnicity data unless there is a particular justification for not doing so. Ethnicity data for New Zealand sites is provided to HDEC at the time of the final report; please collect at a site level if not required for the protocol.
3. The Committee noted that the website should be provided for review prior to going live to participants.

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

1. Please specify that the koha will be offered as a one off at the end of the study.
2. Please be clear around the timing and the ‘how’ of collection of breast milk.
3. Please clarify when the urine samples will be collected.
4. Please review for lay language when explaining lactation and the heel prick.
5. Please clarify the control recruitment. A separate sheet may be easier to provide rather than incorporating relevant information into the existing PIS.
6. Please clarify that there will be a website and please provide information on this.
7. Please include page numbers.
8. Please replace the 0800 4 ETHIC number and replace with the Ministry of Health general enquiry number.
9. Please amend the wording of “sample destruction” to “sample disposal”.

**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 Dr Sotera Catapang and Dr Maree Kirk.

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| **3** | **Ethics ref:** | **2024 FULL 18953** |
|  | Title: | A 3D printed AFO for personalised form and function in patients with movement disorders |
|  | Principal Investigator: | Dr Julie Choisne |
|  | Sponsor: | University of Auckland |
|  | Clock Start Date: | 6 June 2024 |

Dr Julie Choisne and Ms Sara Chami 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 resolved ethical issues

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

1. The Committee noted that the peer reviewer was a senior lecturer but did not mention what institution. The Committee also queried how suggested changes were addressed. The Researchers detailed how they responded to the peer reviewer’s comments in the protocol.
2. The Researchers confirmed the device being trialled would be familiar to participants and will last as long as other available devices.

Summary of outstanding ethical issues

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

1. The Committee noted that in C16 of application form, the possibility of conducting interviews at home is referred to. If so, a safety plan and protocol amendment is required to look after staff going into homes.
2. The Committee noted the response that this study is not collecting ethnicity data. All Researchers should collect good quality ethnicity data unless there is a particular justification for not doing so. Ethnicity data for New Zealand sites is provided to HDEC at the time of the final report.
3. The Committee suggested that Assent forms need an ‘older’ and ‘younger’ age assent forms. Older children can probably understand what you are doing quite well, so best to split them up to cater to comprehension levels.
4. The Committee noted that the University Data Management template was used and that it does not adequately meet the detail required by the Committee and isn’t currently in line with the National Ethical Standards. The Committee suggested use of the [HDEC template on the HDEC website](https://ethics.health.govt.nz/guides-templates-and-forms/data-and-tissue-management-plan-templates).
5. The Committee noted that adverts should include that the ethical aspects of the study have been approved by Northern A HDEC.
6. The Committee queried if there is a chance for the participants to have ongoing access to an investigational device when the device created for the study requires replacement. The Researchers confirmed this is the long-term plan. The Committee requested that the study should be upfront in the information sheets that the study device is expected to last as long as a regular AFO device, and whether the Researchers can assist them to get further device access, and a timeframe for this.

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

All:

1. Please replace University ethics committee contact details with HDECs. These can be found in the [PIS templates](https://ethics.health.govt.nz/guides-templates-and-forms/participant-information-sheet-templates/).
2. The Committee queried use of ‘shank’ and suggested age-appropriate language like ‘leg’.
3. Please include an explanation of compensation for injury. The Committee noted that University of Auckland insurance through their commercial arm should apply.
4. Please add version number to the information sheets.
5. Please add how many people are being recruited, and how long you expect the study to go for.
6. Assent form says a participant can ask for results but this is not in the main body of the information sheet. Please amend.
7. The Committee noted and confirmed that the information sheets do not specify where participants need to go to take part in the study. Please amend.
8. Please state that study will only be occurring in Auckland.
9. Please review for any technical language like ‘mocap’ or other terminology not defined.
10. The Committee requested clarity about where data is being stored, such as on the designated University of Auckland research servers.

Parental PIS:

1. If the participant is only the child, please correct to just “Your child is invited” rather than “You and your child”.

**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).*
4. Please update the data management plan, taking into account the feedback provided by the Committee*. (National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15a).*
5. Please provide a researcher safety plan addressing the concerns raised by the Committee *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.62).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Mr Jonathan Darby and Dr Andrea Forde.

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| **4** | **Ethics ref:** | **2024 FULL 19567** |
|  | Title: | A Phase 2b, Double-Blind, Randomized Extension Study to Evaluate the Long-Term Safety and Efficacy of PTC518 in Participants with Huntington’s Disease |
|  | Principal Investigator: | Dr Tim Anderson |
|  | Sponsor: | PTC THERAPEUTICS, INC |
|  | Clock Start Date: | 6 June 2024 |

Ms Laura Paermentier 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 resolved ethical issues

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

1. The Committee clarified the number of participants in the previous study set to roll over into this extension study. The researcher noted that they intend to consent patients at the last visit of the double-blind study. The participants would have access to the participant information sheet in advance of that visit, prior to consenting.
2. The Committee clarified that there are 2 people of child-bearing potential in the double-blind study and the researchers are monitoring them with pregnancy tests regularly.
3. The Committee clarified that there is no one who identifies as Māori in the parent study.
4. The Committee clarified the psychological and mental health support throughout this study and that the service would be covered by the public system.
5. The Committee clarified the extension study has gone to SCOTT.

Summary of outstanding ethical issues

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

1. The Committee queried if there should be note of herbal, complementary or alternative medicines.

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

1. Please refer to “unborn baby” as a “pregnancy”.
2. Please clarify if there is any risk of seminal fluid containing metabolites and whether the risk of this is actually more than reproductive risk. This should be explained to specify that the risk is not entirely reproductive.
3. Please amend the use of the term “illicit drugs” as this is quite United States-specific.
4. Please include the exclusion of alternative medicines or complementary and herbal medicines.
5. Please remove the tick-boxes from the notification of GP. For this type of study this should be mandatory.
6. Please replace the 0800 4 ETHIC number with the Ministry of Health General Inquiries number per the [HDEC PIS template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-v5.0april2023.doc).

**Decision**

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

* please address all outstanding ethical issues raised by the Committee
* please update the Participant Information Sheet and Consent Form, taking into account the feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
* please update the study protocol, taking into account the feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).*

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| **5** | **Ethics ref:** | **2024 FULL 20202** |
|  | Title: | A Sequential, Randomized, Double-Blind, Placebo-Controlled, Phase 1 Single and Multiple Ascending Dose Study of LTG-305  Administered Orally to Evaluate the Safety, Tolerability, and Pharmacokinetics in Healthy Male and Female Participants 18 to 55 Years of Age. |
|  | Principal Investigator: | Dr Alexandra Cole |
|  | Sponsor: | Novotech (New Zealand) Limited |
|  | Clock Start Date: | 6 June 2024 |

Dr Alex Cole, Miss Kayla Malate, Ms Lucy Druzianic, and Miss Julia O’Sullivan 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 outstanding ethical issues

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

1. The Committee requested that the radio advertisements be amended to reduce the inducements through mention of “Free wi-fi and PlayStation and Netflix”.
2. The Committee requested that the sponsor be encouraged to pursue licensure in New Zealand.

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

1. Please remove mention of “impacting the care you receive” as these are healthy participants.
2. Please amend the schedule of assessments as the foot note for ECG should read “c” and not “e”.
3. Please amend “All these routine samples will be sent to Canterbury Health Laboratories for testing and destroyed…” to “disposed of” instead of “destroyed”. This will keep wording consistent with section 5.1 where it mentions disposal.
4. Please specify the location where the servers for the “secure sponsor-managed database” are.
5. Please specify the location of the NZCR servers.
6. Please replace the 0800 4 ETHIC number with the Ministry of Health General Inquiries number per the [HDEC PIS template.](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-v5.0april2023.doc)
7. Please specify “Auckland Metropolitan Area”.
8. Please provide information detailing other standard/scheduled vaccinations, not just Covid.

**Decision**

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

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

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| **6** | **Ethics ref:** | **2024 FULL 20183** |
|  | Title: | AAA-Shape Pivotal Trial: Abdominal Aortic Aneurysm Sac Healing and Prevention of Expansion |
|  | Principal Investigator: | Dr Andrew Holden |
|  | Sponsor: | Shape Memory Medical Inc |
|  | Clock Start Date: | 6 June 2024 |

Dr Andrew Holden, Ms Cindy Corne, Ms Helen Knight 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 resolved ethical issues

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

1. The Committee clarified that the exclusion of pregnant people from the trial is due to the nature of the intervention and the use of radiation and contrasts. The Committee noted the researcher’s advice that a pregnant person would be very unlikely to appear in the study population.
2. The Committee clarified the length of stay post-procedure.
3. The Committee clarified the protocol for the event of aneurysm growth post-study.
4. The Committee clarified that the device does not contain leachates or toxins.

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 provision of the FDA peer review. The Committee requires this in order to be able to adequately assess whether the methodology has been sufficiently scrutinised, with particular interest in terms of the absorption of the polymer device by the body in the two year timeframe as advised by the Researcher.
2. The Committee noted that the Charter for the Data Safety Management Board was provided in a form that could not be opened by the Committee. Please provide this for review.
3. The Committee requested the data management policies from the Sponsor. This is a requirement for New Zealand ethics approval.

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

1. Please state whether the sac shrinkage quoted in the PIS from studies to date is statistically significant or encouraging etc., if possible.
2. Please clarify that the procedure time will be affected by the insertion of the device.
3. Please clarify if the randomisation will proceed in cases where the procedure may not be possible due to complications.
4. Please remove mention of the pregnant partner in the consent form.
5. Please specify that the blood testing done is additional to the standard of care.

**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 Dr Sotera Catapang and Ms Catherine Garvey.

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| **7** | **Ethics ref:** | **2024 FULL 20371** |
|  | Title: | A Phase 1b Study to Evaluate the Safety, Pharmacokinetics, Pharmacodynamics, and Efficacy of Cavrotolimod Alone and in  Combinations in Subjects with Chronic Hepatitis B Infection. |
|  | Principal Investigator: | Professor Edward Gane |
|  | Sponsor: | PPD, Part of Thermo Fisher Scientific |
|  | Clock Start Date: | 6 June 2024 |

Dr Ed Gane, Ms Lucy Druzianic, Miss Kayla Malate and Ms Julia O’Sullivan 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 resolved ethical issues

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

1. The Committee clarified that there are 2 study drugs, and their separate development histories in different populations.
2. The Committee queried “mental health” listed in the exclusion criteria. The Researcher explained as an innate immune stimulant the study drug causes increases in cytokines including interferon alfa which is known to cause severe psychosis or exacerbation of mood disorders in some people. The Researcher explained interferon alfa as a treatment for Hepatitis B was known to cause suicidality and the exclusion is based on this potential risk.
3. The Researcher clarified Hepatitis D is not a focus of this study and it would be limited to Hepatitis B mono-infection.
4. The Committee queried how participants without a GP would be managed. The Researcher stated all participants would be under secondary care and would have a referring physician in the hospital.
5. The Committee suggested ensuring participants are up to date with all scheduled and recommended vaccines prior to the study commencing.

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 correct the error in section 7.1 of the Data and Tissue Management Plan which suggests participants under 18 will be included.

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

1. Please remove the risks section for BJT-778 in the Part A PIS as participants in this group will not receive it.
2. Please specify if more than one injection may be required and that it may be given in the upper arm, abdomen or thigh as per the protocol.
3. Please specify where the NZCR servers participant data will be stored on are located (eg New Zealand or overseas).
4. Please specify where the Sponsor servers deidentified data will be kept on are located if this is known.
5. Please include the Ministry of Health general enquiries number to the contact section for HDEC queries (0800 400 569).
6. Please amend the heading in 4.3 “risks and disadvantages” to state risks and side effects.
7. Please amend “destruction” of samples to “disposal”.
8. Please refer to “medicine” and not “drug”.
9. Please include HIV and Hepatitis D in the exclusion criteria.
10. Please revise the contraception section to state effective “and” barrier instead of “or”. The Committee suggested removing the requirement to use a diaphragm for a participant with an IUD and taking a pill as this would be an increased burden on those doing so.
11. Please make it clear in the beginning of the Part B PIS that BJT-778 is also investigational and not previously trialled in combination with cavrotilimod.

**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 Data Management Plan (*National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15a*)
* please update the Participant Information Sheet and Consent Form, taking into account the 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:** | **2024 FULL 20396** |
|  | Title: | Open label dose escalation study to evaluate safety, tolerability, pharmacokinetics, and pharmacodynamics of repeated daily oral dosing of YCT-529 for 28 days in healthy men. |
|  | Principal Investigator: | Dr Rohit Katial |
|  | Sponsor: | YourChoice Therapeutics, Inc |
|  | Clock Start Date: | 6 June 2024 |

Dr Rohit Katial, Ms Lucy Druzianic, Miss Kayla Malate and Ms Julia O’Sullivan 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 resolved ethical issues

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

1. The Committee requested information on the discussion with participants around their decision not to have children, particularly younger participants who have not had a vasectomy. The Researcher stated it would be on an individual basis during the informed consent process and modified based on the discussion with that participant. The Researcher stated they would discuss such matters as if the participant has children, if they are likely to want more, their reasons for not having them.
2. The Committee suggested including advertisements aimed toward older men in the target age group, as the current advertisements show younger men with young children.
3. The Committee advised there may be stigma around the concept of male contraception in some communities and suggested the Researcher be mindful of this during the recruitment and advertisement of the study.
4. The Committee queried what support would be available to participants experiencing anxiety or psychological distress if their fertility was permanently affected. The Researcher stated participants who would experience distress at infertility are unlikely to be recruited as this is a risk of participation but any participants experiencing distress related to the dosing would be referred as appropriate and psychological care funded by the Sponsor.
5. The Researcher confirmed if new or unexpected adverse events were observed they would be reported and discussed with the data safety monitoring board.
6. The Researcher confirmed participants can remove the Holter monitor for showering.
7. The Committee requested future submissions that refer to the protocol in the HDEC application specify which page number.
8. The Researcher clarified 50 participants would be recruited worldwide with a number from Australia and New Zealand so the exact number of New Zealand participants is not known as the study would involve competitive recruitment between sites.
9. The Committee advised that as participants would give sperm samples at a fertility clinic, locality authorisation would be 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 requested the informed consent process involves face-to-face discussion and is not solely in reliance on NZCR’s e-consent process in this study. The Committee suggested consulting an expert in fertility issues to formalise the questioning during the screening process. The Committee requested an update to the protocol to detail the interview during screening.
2. The Committee queried if the mandatory sperm samples would be stored at one clinic or if there are multiple sites for this. The Researcher explained this is to be finalised and clarified that samples will only be stored for the stated 10 years if the participant’s results had not returned to normal by the end of the study. The Committee requested this is made clear in the information sheet as well as information explaining if the sample will be kept in the event of participant withdrawal.
3. Please update Section 9.2 of the Data Management Plan (DMP) to specify where the deidentified database is located.
4. The Committee queried the lengthy restrictions on alcohol, caffeine and exercise and the rationale behind them. The Researcher stated the alcohol restriction is due to kidney and liver function during the initial dosing period and for one month after. The exercise restriction is because exercise elevates CK levels which can make it difficult to observe a drug effect on muscle and the liver. The caffeine restriction is due to one case of ventricular ectopic observed in phase 1 though this is not believed to be related to the study drug. The Committee requested this information is included in the information sheet so participants understand why they must abstain from these.

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

1. Please specify where the NZCR servers participant data will be stored on are located (eg New Zealand or overseas).
2. Please specify where the servers deidentified data will be stored on are located.
3. Please be consistent when referring to participants (healthy males, healthy participants, healthy male volunteers).
4. Please specify how kidney and liver function will be monitored (eg blood tests).
5. Please refer to the study drug as an ‘investigational medicine’.
6. Please update the description of reducing fertility on page 11 to acknowledge a decrease in motility and morphogenesis as well as sperm count.
7. Please revise the contraception section to state effective “and” barrier instead of “or”.

**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*).
4. Please update the Data Management Plan (*National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15a).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Dr Maree Kirk, Mr Derek Chang and Ms Catherine Garvey.

## General business

1. The Chair reminded the Committee of the date and time of its next scheduled meeting:

|  |  |
| --- | --- |
| **Meeting date:** | 16 July 2024 |
| **Zoom details:** | To be determined |

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 5:01pm.