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| **Committee:** | Southern Health and Disability Ethics Committee |
| **Meeting date:** | 09 July 2019 |
| **Meeting venue:** | Sudima Hotel, Christchurch Airport, 550 Memorial Drive, Christchurch |

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| **Time** | **Item of business** |
| 11:30am | Welcome |
| 11:35am | Confirmation of minutes of meeting of 11 June |
| 11:40am  11:45am | General business:  Noting section  New applications (see over for details) |
| 11:45 – 12:00pm  12:00 – 12:10  12:10 – 12:35  12:35 -1:00  1:00 – 1:25  1:25 – 1:50  1:50 – 2:15  2:15– 2:40  2:40 – 3:05 | i 19/STH/119 (Raewyn/Mira)  ii 19/STH/123 (Raewyn/Jean)  iii 19/STH/115 (Sandy/Nicola)  iv 19/STH/91 (Sarah/Jean)  v 19/STH/121 (Raewyn/Mira)  vi 19/STH/128 (Sandy/Jean)  vii 19/STH/127 (Sarah/Nicola)  Substantial amendments  viii 15/STH/47/AM06 (Sandy/Jean)  New applications  ix 19/STH/124 (Sarah/Devonie)  x 19/STH/125 (Sarah/Devonie)  xi 19/STH/126 (Sarah/Devonie) |
| 3:05pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |  |
| Ms Raewyn Idoine | Lay (consumer/community perspectives) | 27/10/2015 | 27/10/2018 | Present |  |
| Dr Sarah Gunningham | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | Present |  |
| Assc Prof Nicola Swain | Non-lay (observational studies) | 27/10/2015 | 27/10/2018 | Present until 2:15pm |  |
| Dr Devonie Waaka | Non-lay (intervention studies) | 18/07/2016 | 18/07/2019 | Present |  |
| Ms Sandy Gill | Lay (co-opted) |  |  | Present |  |
| Assc Prof Mira Harrison-Woolrych | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | Present until 3:05pm |  |
| Dr Paul Chin | Non-lay (intervention studies) | 27/10/2018 | 27/10/2021 | Apologies |  |
| Professor Jean Hay-Smith | Non-lay (health/disability service provision) | 31/10/2018 | 31/10/2021 | Present |  |

## Welcome

The Chair opened the meeting at 11:45am and welcomed Committee members, noting that apologies had been received from Dr Paul Chin, that Assc Prof Nicola Swain would only be able to attend until 2:15pm, and that Assc Prof Mira Harrison-Woolrych would only be attending until 3:05pm.

The Chair noted that it would be necessary to co-opt members of other HDECs in accordance with the Standard Operating Procedures. Ms Sandy Gill confirmed her eligibility, and was 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 11 June were confirmed.

## New applications

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| **1** | **11:45 – 12:10** | **Ethics ref:** | **19/STH/119** |  |
|  |  | Title: | A Comparative Clinical Evaluation of a New TECNIS Presbyopia-Correcting Intraocular Lens Against A Trifocal Intraocular Lens |  |
|  |  | Principal Investigator: | Dr Dean Corbett |  |
|  |  | Sponsor: | Johnson & Johnson Surgical Vision, Inc. |  |
|  |  | Date submitted: | 26 June 2019 |  |
|  |  | Clock Start Date: | 27 June 2019 |  |

Dr Dean Corbett, Ms Naoko Chapman and Ms Angelica was present by teleconference 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. Implanted lenses are an alternative treatment for optometric patients who do not wish to wear glasses, but products developed so far all result in night-time vision disturbances, although they have been decreasing.
2. The study will evaluate the patient-reported outcomes with regard to unwanted night time phenomena that occur as a result of having implantation of a newly developed lens which is hoped to produce fewer night-time disturbances. These results will be compared against a commonly used standard-of-care model.

Summary of resolved ethical issues

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

1. The Committee enquired as to how the researchers would invite patients of theirs to participate, and how they would ensure there is no undue pressure on them. The Researcher explained that patients will be approached by the one of the investigators, and if they are interested in the study they will be given a PIS to take home. If they then wish to participate they may call a research assistant to speak with.
2. The Committee asked whether there may be risks to participants involved with using a new optical lens not mentioned in the PIS. The Researcher explained that the only risk is in the design of the diffractive pattern on the lens: the lens material and shape are otherwise the same as in previous products.

Summary of outstanding ethical issues

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

1. The Committee queried the justification for the travel remuneration offered, suggesting it may be low for the Auckland region. The Researcher explained that the amount offered was a standard amount, but that extra remuneration was available for those with specific needs, as mentioned in the PIS.
2. The Committee asked, if a patient is enrolled but is unable to receive the study lens, will they be given another lens at no extra cost? The Researcher confirmed that a standard lens will be inserted at no cost, and that the participant will then be exited from the study. The Committee expressed concern that the participant may unexpectedly end up with one lens and have to wait for another lens to be inserted separately, and requested that this be made explicit in the PIS.
3. The Committee enquired as whether any private health insurance costs might be incurred for participants. The Researcher explained that the sponsor would only fund up to $5000 of the surgery, and any remaining cost would need to be paid by health insurance. The Committee asked if the insurance companies will be willing to pay for this cost, and the Researcher responded that they are still waiting to hear back from Southern Cross. This information must be explicitly stated in the PIS.

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

1. Please ensure all language is as objective as possible and remove any potentially promotional language, such as “in both cases you will get a product that provides useful vision across a range of distances” (Page 6).
2. Please remove the reference to “a good subject”, replacing with, for example “if you meet our criteria”.
3. Please replace ‘subject’ with ‘participant’ or ‘person’ throughout the document.

Decision

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

* Please provide a letter from Southern Cross, detailing whether the costs incurred on participants in this trial would be covered by health insurance.
* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee.

This following information will be reviewed, and a final decision made on the application, by Dr Sarah Gunningham and Prof Mira Harrison-Woolrych.

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| **2** | **4:20** **– 4:45** | **Ethics ref:** | **19/STH/123** |  |
|  |  | Title: | ACTICCA-1 |  |
|  |  | Principal Investigator: | Dr Amanda Ashley |  |
|  |  | Sponsor: | NHMRC, Clinical Trials Centre |  |
|  |  | Date submitted: | 26 June 2019 |  |
|  |  | Clock Start Date: | 27 June 2019 |  |

The Committee did not require any member of the study team to be present for the discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This study aims to determine if cisplatin and gemcitabine, the regimen used for palliative chemotherapy in unresectable gallbladder cancer, is superior to the current standard of care regimen of adjuvant capecitabine in patients following resection of their gall bladder cancer. The primary endpoint will be disease-free survival, with secondary endpoints measuring disease free survival rate at 24 months, recurrence free survival, overall survival, safety and tolerability of adjuvant chemotherapy, quality of life, function of biliodigestive anastomosis (in terms of surgical revision, requirement for PTCD), rate and severity of biliary tract infections, patterns of disease recurrence and locoregional control.
2. This is a multi-centre study with three participants in New Zealand.

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 for the initial approach to patients to be made by a member of the patient's clinical care team

Summary of outstanding ethical issues

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

1. It was not clear, based on the answers in the application form, whether Investigators from other sites will be involved. If so, please provide a list of those investigators.
2. Please ensure that, if a participant withdraws, the study doctor obtains consent to continue to collect information.

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

1. Please amend the title and short title to make them meaningful to lay readers.
2. Please ensure that formatting is consistent throughout the document.
3. If New Zealand sites are only planning to recruit post-surgery, it is suggested that the pre surgical screening section is deleted.
4. Page 3: please state how many pages are in the form.
5. Page 4: please provide an estimate of how long the listed follow-up visits will take.
6. Page 5: it is noted that optional blood samples are taken at screening, post-op and at recurrence. Are these only for participants who provide separate consent? If so, please remove from the main body of the PIS and include in the addendum (see point X below).
7. Page 6: please provide the frequency for ‘common’, i.e. common affects 1:10, less common affects 1:100.
8. Page 8: please remove information about optional testing from the body of the main PIS. This should be included in a separate addendum after the main consent.
9. Page 10: please state that coded health information may be provided to other researchers for future research.
10. Page 12: please amend the contact information to provide Maori support details (Maori advisors are not available through the Health and Disability Commission).
11. Page 13 (consent form): please remove the section about optional testing from the main consent form, and include under the addendum (see point X above).
12. Please add an optional tick box to the consent form for data to continue to be collected from the participant’s health record if he or she withdraws.
13. It is suggested that headings are added for the different regimens, for clarity.

Decision

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

* If Investigators at other sites are involved in the study, please provide a list of the lead Investigators at each site with the next annual progress report.
* Please update the protocol to ensure that, if a participant withdraws, consent is sought for the future collection of data.
* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee.

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| **3** | **12:10 – 12:35** | **Ethics ref:** | **19/STH/115** |  |
|  |  | Title: | Long term effects of heavy cannabis use |  |
|  |  | Principal Investigator: | A/Prof Joseph M. Boden |  |
|  |  | Sponsor: |  |  |
|  |  | Date submitted: | 05 June 2019 |  |
|  |  | Clock Start Date: | 27 June 2019 |  |

Dr James Foulds and Tracy Melzer were present in person 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 is an observational case control study of the long term effects of heavy cannabis use in 50 participants. The study will assess whether there are linkages between heavy cannabis use in adolescence and early adulthood, and an array of outcomes at age 42, among participants drawn from the Christchurch Health and Development Study, a longitudinal study of over 1000 people born in Christchurch in mid-1977. The study will obtain data from brain and cardiac MRI, cognitive testing, genetics and other physical health measures. These data will be used to compare health outcomes between a sample of 25 participants with a history of heavy cannabis use, and a matched control sample of 25 participants without past cannabis exposure. The study will draw on the existing extensive database of exposure and outcome data for participants in the CHDS cohort to determine whether heavy cannabis use is associated with adverse health outcomes at age 42.

Summary of resolved ethical issues

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

1. The Committee cautioned the researchers to be wary of the potential risk of stigmatisation in collecting ethnicity data for heavy Cannabis use, particularly if Māori turn out to be over-represented in the heavy use participants.
2. The Committee noted the cultural issue for Māori of whakamā, particularly for heavy users where their Whānau may not know of the extent of their use.
3. The Committee noted an inconsistency between the application form and PIS regarding whether the potential participant was a cannabis user now, and if they were a heavy cannabis user as an adolescent. The Researchers explained that they ideally want to recruit people who are heavy cannabis users now, but, if that makes recruitment too difficult, then previous heavy users would be included.
4. The Committee enquired as to how source data for MRI imaging will be protected. The Researchers explained that the data will be coded and a key held by one member of the research team.

Summary of outstanding ethical issues

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

1. Due to question D of the application form being answered incorrectly, the form did not produce the following questions – please answer them in a response letter:

**r.1.1**. Briefly and in plain English, please describe:

* + the procedures to be undertaken by participants in your study, and
  + any risks associated with these procedures that potential participants may reasonably wish to be informed of.

Do not describe procedures that will be undertaken as part of normal clinical care regardless of participation in your study, or the risks of such procedures.

**r.1.2.** Will you seek consent from participants to inform health practitioners with responsibility for their health care that they are taking part in your study? (Yes/No – if no, please explain why)

**r.1.3.** Will your study involve withholding standard treatment from participants? (Yes/ No)

**p.1.1.** Briefly and in plain English, please describe what taking part in your study will involve for participants.

**p.1.2.** Will **all** participants in your study give their informed consent to participate?

**p.1.9.** Will informed consent be recorded in writing? (Yes/No) If no:

**p.1.9.1.**Please describe how participants’ informed consent will be recorded.

**p.2.1.** Briefly explain the process by which potential participants in your study will be provided with information on the study, have the opportunity to ask questions, and asked to give their informed consent.

**p.2.3.** How have you checked that the participant information sheet is appropriate for your study population?

**p.2.4.** How many words does your participant information sheet contain?

**p.2.5.** What is the Flesch Reading Ease Score for your participant information sheet?

**p.2.6.** Does your study involve deliberately withholding or concealing information from participants? (Yes/No)

**p.2.7.** How will you ensure that participants receive information that becomes available during the study and that may be relevant to their continued participation?

**p.2.8.** Will you inform participants of the results of your study? (Yes/No)

**p.2.9.** Please *either* explain how you will inform participants or explain why you do not intend to do so.

**p.3.1.** Please explain how potential participants will be identified and approached in a way that ensures they can give informed consent free from undue influence.

**p.3.2.1.** Please explain how your study’s informed consent process takes the needs of these potentially vulnerable people into account.

**p.3.2.2.** Will informed assent also be sought from people responsible for the welfare of potentially vulnerable people involved in your study? (Yes/No – if yes, please explain)

**p.3.3.** Will participants receive any payments, reimbursement of expenses or any other benefits or incentives for taking part in your study? (Yes/No)

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

1. Please upload a PIS for future unspecified use of tissue (FUR). You may wish to refer to the HDEC template:  
   https://ethics.health.govt.nz/system/files/documents/pages/fur\_piscf\_template.doc
2. In the main PIS, please clarify that you may be doing genetic testing (and explain what this is in lay terms), and that tissue may be sent overseas.
3. Please specify the tissue bank in which samples will be stored, as well as its location.
4. The referral of incidental findings to a participant’s GP should be mandatory – please remove any reference to it being optional, and state “test findings that may be important to my health” instead of “incidental findings”.
5. Please proofread the PIS documents, correcting for errors and using clear formatting.
6. Please explain in the main PIS how you will be following up to get participants’ feedback.
7. Add the Māori and HDEC contact phone numbers to the end of the form.
8. The Committee suggested that the participant groups be broken up into recent heavy cannabis users currently suffering withdrawal symptoms, recent users who are no longer suffering withdrawal symptoms, and previous heavy users who are no longer suffering withdrawal symptoms. The risks for each should be explained.
9. Please state that imaging information will be stored in a coded form only accessible by the study staff for the duration of the study.

Decision

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

* Please complete the application questions outlined above and submit in a cover letter.
* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee.

This following information will be reviewed, and a final decision made on the application, by Ms Sandy Gill and Dr Sarah Gunningham.

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| **3** | **12:35 -1:00** | **Ethics ref:** | **19/STH/91** |  |
|  |  | Title: | Microdosing LSD |  |
|  |  | Principal Investigator: | AP Suresh Muthukumaraswamy |  |
|  |  | Sponsor: | The University of Auckland |  |
|  |  | Date submitted: | 02 May 2019 |  |
|  |  | Clock Start Date: | 02 May 2019 |  |

Professor Suresh Muthukumaraswamy was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This study is a randomised controlled trial of repeated micro-doses of LSD under schedules similar to those suggested in the ‘grey’ literature. 40 healthy volunteers will be randomised to first receive repeated doses of either inactive placebo or LSD (10 μg oral) under double-blind conditions in a crossover design. A variety of physiological and psychological measures will be recorded at baseline and after completion of each of two six-week dosing regimens. Measures will include a validated personality scale, tests of creativity and attention, basic physiological measures (heart rate, blood pressure), sleep and activity tracking, and participant self-reports. Electroencephalography and magnetic resonance imaging will be used to directly measure brain function and structure in each participant before and after treatment. This should will an evaluation of the purported benefits of psychedelic micro-dosing and will be relevant to the question of whether micro-dosing may be a viable alternative treatment regimen for depression or addiction.

Summary of resolved ethical issues

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

1. The Committee noted that although a legal opinion had been requested from the Ministry of Health, as it had not been received the Committee could not consider it, so would judge the application based on the legal advice given by the researchers.
2. The Committee accepted the legal opinion provided by the researchers.

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 although the study will be advertised, no recruitment advertisements had been submitted.

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

1. Please remove the yes/no tick boxes from the consent form for all statements that aren’t truly optional, i.e. those where a participant could select ‘no’ and still participate in the study.
2. Page 3:
   * Please correct “on your 3rd visit six blood samples (10mL each – a teaspoon)”. 1 teaspoon = 4.98mL, therefore 10mL = 2 teaspoons.
   * “You should be aware that once you have been informed that a clinical abnormality has been detected through performing a scan on you this could affect your ability to obtain insurance whether or not you take the matter further.” This information is stated twice, once in a separate bullet point, but is also in the preceding paragraph. Please amend accordingly.

Decision

This application was *approved* by consensus, on the condition of a favourable legal opinion from the Ministry of Health, and subject to the following non-standard conditions:

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee.
* Please submit the advertising documents separately for review as an amendment. Advertising material cannot be used until those materials have been approved.

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| **4** | **1:00 – 1:25** | **Ethics ref:** | **19/STH/121** |  |
|  |  | Title: | Midodrine as an Adjunctive VasoprEssor for Refractory Hypotension in Intensive Care (MAVERIC) Study |  |
|  |  | Principal Investigator: | Dr Paul Young |  |
|  |  | Sponsor: |  |  |
|  |  | Date submitted: | 26 June 2019 |  |
|  |  | Clock Start Date: | 27 June 2019 |  |

Dr Paul Young was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This study is looking at administration of Midodrine to treat low blood pressure, allowing patients who are already on the path to recovery to leave the intensive care unit more quickly. The study will compare the use of Midodrine and vasopressors with vasopressors alone (the standard of care).

Summary of resolved ethical issues

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

1. The Committee queried the lack of a placebo arm. The Researcher responded that as it is an unfunded study, and using a placebo would be very expensive, this option is not feasible. The Committee agreed that that this is reasonable, as it is a pilot study, but if the study were to be expanded that it then should be blinded.
2. The Committee questioned whether a member of the patient’s clinical care team will first approach the patient to ask about participating in the study, before a member of the study team. The Researcher confirmed this.

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

1. Please include the frequencies of the side effects (i.e. what does ‘common’ mean?).
2. Please add on page 2: “you have been chosen to participate in this study because you are already receiving intravenous vasopressors”.
3. Consent form:
   * The consent form states that, in the event of a participant withdrawing from the study, analysis of data collected up to the point pf withdrawal is optional. Please ensure that this information is outlined in the PIS.
   * Please remove the clause on pregnancy, accepting risk and taking responsibility.
   * The consent form states that regulatory authorities might audit the study – this is inconsistent with PIS, which only states that HDECs will review the study. Please make sure this is consistent.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee.

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| **5** | **1:25 – 1:50** | **Ethics ref:** | **19/STH/128** |  |
|  |  | Title: | Long-term safety and efficacy of Bimatoprost SR |  |
|  |  | Principal Investigator: | Professor Anthony Wells |  |
|  |  | Sponsor: | Allergan Australia Pty Ltd |  |
|  |  | Date submitted: | 27 June 2019 |  |
|  |  | Clock Start Date: | 27 June 2019 |  |

Professor Anthony Wells was present by teleconference 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 is an extension study of Bimatoprost SR in open angle glaucoma or ocular hypertension. There are six participants in New Zealand, 600 patients in 600 countries worldwide, and no ethics approval to date.

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, for the future reference of the Researcher, that the answer to question p.4.1 of the application form was not adequate. If the study is not designed to reduce inequities for Māori this should be stated; the Treaty should not be used to defend it. The Committee also asked that macrons be used when spelling ‘Māori’.
2. In future applications, please upload the full files (not in ZIP format), as these are difficult to access for review.

Summary of outstanding ethical issues

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

1. No evidence of scientific peer review was submitted to the Committee. This is required for applications to be considered.
2. Although this cannot be addressed in the present application, for future reference the Committee noted that several of the questions on the application form were answered incorrectly (for example: question D “does your study involve human participants” was answered “no”. The incorrect response prevented the form from populating other relevant questions later in the form. Questions a.1.5, a.2.2.1, b.2.1, b.2.2.1, b.4.2, r.2.1.1, r.2.3.1, f.2.5 were also answered incorrectly.
3. The Committee noted that the cultural section of the application form was not filled out with clear reference to the present study, and in particular did not identify if any participants may be Māori based on enrolment in the lead-in trials.

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

1. Page 1 Introduction: please state that patients are invited to take part because they participated in a lead-in study.
2. Page 2: Please expand the overview of study participation, e.g. including the number of visits, the total time period, the number of participants, when and for what reasons the study may be terminated, for what reasons the study doctor may withdraw a participant from the study, if the previous dose strength will be discussed, and so on. Please do this while ensuring that it follows a logical order.
3. “Through month 12” sounds like an Americanism that doesn’t make sense in a NZ context, please change the language.
4. Page 3. Call them treatment cycle 1 and treatment cycle 1. The PRN abbreviation is a needless acronym. You talk about different visits with different names and it is not clear how this works; it seems you want all participants to be followed for 24 months regardless of whether they have more study drug or not, and if they have 1 or 2 more administrations of the study drug you will ask them to come for more visits.
5. The list of investigations/tests is lengthy and the reader has to do a lot of work to find out how many appointments this study might entail. The participant burden is not at all clear from this. A table may help - the relevant information is actually on page 7.
6. If the Committee’s understanding is correct, all participants from previous studies are eligible to participate in the extension, for assessment of safety and longer term effect. In addition, if they agree, some participants in the extension study will be offered 1 or 2 further doses of the drug as needed (at the same dose they’ve already had in the prior study), depending on how many doses they’ve already had and whether or not they needed other treatment if the drug did not work for them. This is not readily understood as currently presented in the PIS.
7. Page 3: Please proof-read, reducing the use of jargon and increasing overall readability. Please add a table to give an idea of what is required and when.
8. Page 4: the application form states no tissue will be collected, yet the PIS states that ocular fluid will be collected during surgery and will become the property of Allergan. Please correct this inconsistency, and if tissue will be collected then clarify:
   * What it will be used for.
   * If research could include genetic/genomic testing.
   * Where it will be analysed/stored (and whether samples will be sent overseas)
   * How confidentiality will be maintained (for example, how samples will be labelled)
   * How long it will be stored for
   * If participants have the right to withdraw samples that have been collected.
9. The usual statement about the special nature of body tissue is not here and must be included. (see <https://ethics.health.govt.nz/system/files/documents/pages/piscf-template-february-2019-v2.0-150719.doc>) It should also state whether a karakia is possible at time of donation.
10. Page 5 (additional study visits after 24 months): please clarify how long participants are being asked to consent to be followed. Are these continued visits the researcher’s choice? What are they for? This would better be moved to page 7.
11. Page 5 (study administration procedure): is this all the information that was provided in the original study? If it is part of the present study it needs greater detail.
12. Page 6: are GPs sent a list of prohibited con meds?
13. Page 6: what does the statement “you can only take part in one location” mean? Also re-word “these medications and procedures are not allowed through rescue in your study eye (This section is application if you study eye has not been rescued)”
14. Page 7: there is unnecessary repetition in the section titled “other relevant information about the research project” (number of participants and countries, number of visits - timing of visits should go with the information about visits).
15. Pages 7/8: move inclusion and exclusion criteria up to page 2. This is too long to read to find out you’re not eligible.
16. Page 8: the risk section is inadequate. Please organise risks into frequencies and use bullet points.
17. Page 10: please amend the ‘what happens if I become pregnant?’ section, ensuring that it has all the information laid out in the HDEC template (<https://ethics.health.govt.nz/system/files/documents/pages/template-for-reproductive-risks-in-participant-information-sheets-sep17.docx>).
18. Page 11 does not have the recommended contraception statement for women, please refer to the above link. Should there also be information for male participants with a female partner who becomes pregnant? If yes, please include.
19. Page 13: please state the reimbursement amount.
20. P15. Must supply Māori support details.
21. P17. Which samples are being sent overseas? Occular sample? Blood? Urine? What?
22. Check throughout PIS for orphan headings – there are several.

Decision

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

* In order to meet established ethical standards, health and disability research must be scientifically valid. Researchers and sponsors must ensure that the scientific validity of proposed research has been peer-reviewed before an application is made to an HDEC (*Standard Operating Procedures for HDECs* para *11*).
* Applications should only be validated if all relevant questions in the application form have been answered in a manner that is reasonably likely to allow the HDEC to make a final decision on the application the first time it is considered (*Standard Operating Procedures for HDECs* para *42.3*).
* Investigators should effectively communicate to participants the purpose and practical implications of all key study features, including any randomisation, placebo control or blinding (*Ethical Guidelines for Intervention Studies* para *6.12*)
* Investigators are responsible for designing and conducting studies to maximise the validity and quality of participants’ informed consent. Ethics committees are responsible for checking that proposed study information sheets and consent forms enhance informed consent of this nature. (*Ethical Guidelines for Intervention Studies* para *6.13*)

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| **6** | **1:50 – 2:15** | **Ethics ref:** | **19/STH/127** |  |
|  |  | Title: | BRII-179-001: Safety and activity of BRII-179 in CHB |  |
|  |  | Principal Investigator: | Dr Tien-Huey Lim |  |
|  |  | Sponsor: | Brii Biosciences |  |
|  |  | Date submitted: | 26 June 2019 |  |
|  |  | Clock Start Date: | 27 June 2019 |  |

Cameron Shauer and Mrs Catherine Howie was present by teleconference 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 will assess the safety and tolerability of two dose levels of BRII-179 in people without significant liver damage but with CHB infection. It will also compare the antiviral activity of BRII-179 administered via intramuscular injection, with and without low dose interferon alfa (IFN-α), which slows the growth of viruses and boosts the immune system response.
2. Participation will last up to 30 weeks and include: a screening period (up to 6 weeks), a 12 week treatment period and 12 weeks follow-up. Participation requires 9 study visits, each of 1-5 hours depending on procedures required. Between visits, participants complete diary cards and are contacted by phone to review diary cards and adverse events (AEs).
3. This study is looking at the safety, tolerability and antiviral activity of this study drug. There will be twee arms, one for 20 microgram doses and one for 40. Each arm will have two comparison groups: one of the study drug only and the other of the study drug in comparison IFN-α (standard of care.

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 Researchers have experience providing first-in-human medicines before, and the Researchers confirmed that they have experience providing quite similar first-in-human medications.

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 enquired as to the following section in paragraph two: “if you have suicidal ideas, please contact study doctor” and in particular what kind of risks there were. The Researcher explained at higher doses interferon has caused mood disturbance. Furthermore they explained that any with significant mood disturbance will be excluded from the study. The Committee asked how a mood disturbance will be established, and the researchers admitted that this had not been discussed by the research team.
2. The Committee questioned the method of sentinel dosing, which would potentially permit participants in Cohorts B and C to receive the investigational drug at the same time, rather than staggering dosing of the investigational drug by 24 hours.
3. The Committee questioned the rationale for monitoring participants for only one hour post first dose, given this is a first in human study.
4. The Committee asked for further information about the composition and terms of reference for the internal data safety monitoring committee.
5. On page 8, the following is stated: “the tests may reveal that you have previously used illegal drugs…. In the event that [Site name] is required to disclose that information, it may be used against you in legal proceedings or otherwise.” The Committee enquired as to the circumstances in New Zealand in which the Researchers would be required to disclose that information.

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

1. Please add a warning box, in bold page, on page 1, stating that this is a first in man study.

**This is the first time <<study drug>> will be studied in humans.**

**You may not receive any health benefit from the study drug; but there are risks of you having a drug reaction, injury or illness.**

1. Risk frequencies definitions appear to all be the same and are confusing. Please amend this.
2. Please tidy the formatting of the document, for example making the table fit to one page.
3. Reproductive risks for men: please use the same information as for women (either refer them to the information provided for women or repeat it for men). It is recommended that you refer to the HDEC template: <https://ethics.health.govt.nz/system/files/documents/pages/template-for-reproductive-risks-in-participant-information-sheets-sep17.docx>
4. Page 3: it is stated that the drug is given in 4 doses – please change this to “20 micrograms for four doses”.
5. Pages 14-15: It is unclear who has access to uncoded data and who has access to coded data. Please make it clear that uncoded data will be accessed only for audit purposes (and will not be removed from the site); and that only coded study data will be sent off site.
6. Page 6: explain what an ECG is.
7. Page 7: section 5 should be moved under section 3. It is part of the overall information about the study.
8. Page 12: bold the information about potential psychiatric risks.
9. The Committee asked whether there is an upper limit to the reimbursements outlined on page 7, and that this needs to be stated in the PIS.
10. Please confirm that the year of birth only will be sent to the sponsor.
11. The regime on page 3 states: “you’ll be randomized to one of the following 3 treatments”. This does not make clear whether a participant will be randomized to one of the options within part 2, or just to either part 1 or 2.
12. There are too many acronyms for a lay reader – please simplify the language.
13. Please update the emergency phone number.
14. Pregnancy PIS:
    * Please remove the compensation statement.
    * Page 2: the risks of the study drug are not known, so please remove information about the potential risks miscarriage, foetal death etc. These are distressing and unnecessary as the participant is already pregnant and this discussion should be had in person.
15. Consent form: please state if an interpreter is available.

Decision

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

* Please submit a cover letter addressing outstanding ethical issues 5-8.
* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee.

This following information will be reviewed, and a final decision made on the application, by the full committee.

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| **8** | **2:40 – 3:05** | **Ethics ref:** | **19/STH/124** |  |
|  |  | Title: | Comparison of the blood levels of two forms of oxycodone/naloxone tablets under fasting conditions. |  |
|  |  | Principal Investigator: | Dr Noelyn Hung |  |
|  |  | Sponsor: | AU Pharma Pty Ltd |  |
|  |  | Date submitted: | 26 June 2019 |  |
|  |  | Clock Start Date: | 27 June 2019 |  |

Dr Noelyn Hung and Mrs Linda Folland were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This study is evaluating the bioequivalence, by comparing the rate and extent of absorption, of the test formulation 1 x 5/2.5 mg oxycodone/naloxone tablet (AUPharma, Australia) with 1 x 5/2.5 mg Targin® tablet (Mundipharma, Australia) in healthy subjects under fasting conditions.

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 whether this or any related drug had been approved in New Zealand. The Researchers confirmed that MedSafe has reviewed the study.
2. The Committee noted that in answering question r.1.1 of the application form, which asks about the risks of the study, the Researchers had not included the risks of the medicines.
3. The Committee noted that question p.2.7 of the application form, which asks about how participants will be made aware of important new information that becomes available in the study, had not been appropriately answered. They requested that in future applications, this information (such as that which was included in the PIS) be written in the application form.
4. The Committee asked whether the Researchers used a formula for calculating reimbursements, to ensure that they are determined in a consistent fashion. The Researchers confirmed that they did use a formula and could provide it to the HDEC.

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 answering question p.2.8 of the application form, which asks “will you communicate the results of the study to participants”, the Researchers answered “no, the results will not be communicated to the participants…the results of the trial will be on a clinical trial registry”. The Committee expressed that this was not sufficient, and that all participants need to be able to receive a lay summary of the results. Please add an optional tick box to the consent form for this, and also provide evidence of the sample lay summary letter.

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

1. The ‘risks’ section is not complete, for example common disorders identified in post marketing risk experience summarised in the provided IB have not been included. Please review the IB and amend accordingly.

Page 5: please add “is not permitted” following “the following requirements must be observed in the study… use of cocaine, marijuana”.

1. After the drugs paragraph it states “you must not take from taking any prescription medication used with the intention to treat a condition”. Please make this an exclusion criterion (on page 3).

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee.
* Please ensure a copy of the lay summary letter is uploaded when the final report for this study is submitted to HDEC.

This following information will be reviewed, and a final decision made on the application, by Dr Sarah Gunningham and Dr Devonie Waaka.

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| **9** | **3:05 – 3:30** | **Ethics ref:** | **19/STH/125** |  |
|  |  | Title: | Comparison of the blood levels of two forms of oxycodone/naloxone tablets under fed conditions. |  |
|  |  | Principal Investigator: | Dr Noelyn Hung |  |
|  |  | Sponsor: | AU Pharma Pty Ltd |  |
|  |  | Date submitted: | 26 June 2019 |  |
|  |  | Clock Start Date: | 27 June 2019 |  |

Dr Noelyn Hung and Mrs Linda Folland were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This study is evaluating the bioequivalence, by comparing the rate and extent of absorption, of the test formulation 1 x 5/2.5 mg oxycodone/naloxone tablet (AUPharma, Australia) with 1 x 5/2.5 mg Targin® tablet (Mundipharma, Australia) administered 12 hours apart in healthy male and female subjects under fed conditions.

Summary of ethical issues

The resolved and outstanding ethical issues for this study are the same as for 19/STH/124.

Decision

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

* Please ensure a copy of the lay summary letter is uploaded when the final report for this study is submitted to HDEC.
* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee.

This following information will be reviewed, and a final decision made on the application, by Dr Sarah Gunningham and Dr Devonie Waaka.

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| **10** | **3:30 – 3:55** | **Ethics ref:** | **19/STH/126** |  |
|  |  | Title: | Comparison of the blood levels of two forms of oxycodone/naloxone tablets under steady state conditions. |  |
|  |  | Principal Investigator: | Dr Noelyn Hung |  |
|  |  | Sponsor: | AU Pharma Pty Ltd |  |
|  |  | Date submitted: | 26 June 2019 |  |
|  |  | Clock Start Date: | 27 June 2019 |  |

Dr Noelyn Hung and Mrs Linda Folland were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This study is evaluating the bioequivalence, by comparing the rate and extent of absorption, of the test formulation 1 x 5/2.5 mg oxycodone/naloxone tablet (AUPharma, Australia) with 1 x 5/2.5 mg Targin® tablet (Mundipharma, Australia) in healthy subjects at steady state.

Summary of ethical issues

The resolved and outstanding ethical issues for this study are the same as for 19/STH/124, with the exception of the following changes to the Participant Information Sheet and Consent Form:

1. The Committee noted that as participants have to fast for 4 hours before/after each dose, they are not allowed to eat for 16 hours a day, which could make it difficult to get meals. The PIS also states that non-citrus fruits are available in the evenings, however that is during the fasting time. Please make the extent of fasting very clear.
2. The PIS states “you will receive the test formulation 5 times and reference formulation 5 time, the order in which you will receive each of the formulations will be randomly assigned”. Please clarify that participants will get blocksof 5.

Decision

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

* Please ensure a copy of the lay summary letter is uploaded when the final report for this study is submitted to HDEC.
* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee.

This following information will be reviewed, and a final decision made on the application, by Dr Sarah Gunningham and Dr Devonie Waaka.

## Substantial amendments

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| **7** |  | **Ethics ref:** | **15/STH/47/AM06** |  |
|  |  | Title: | A National Audit of Hereditary and Aquired Angioed |  |
|  |  | Principal Investigator: | Dr Karen Lindsay |  |
|  |  | Sponsor: |  |  |
|  |  | Date submitted: | 20 June 2019 |  |
|  |  | Clock Start Date: | 12 June 2019 |  |

Dr Karen Lindsay was present by teleconference 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 amendment is to add a new population of participants, who are the children of participating adults. The same information will be collected from the children group as from the original adult population.
2. All these children have hereditary angioedema.

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 sponsor’s involvement in the study, and expressed concern that the sponsor might be using the study to promote their medication. The Researcher explained that although the study is funded by the sponsor, the aim is not to encourage participants to take the medication, but to find out who is using it; what their experiences are; how severe their attacks are and so on, in order to assess the patient population’s needs. The Researcher further explained that the information from the study would be presented to the sponsor in a summarised, de-identified form only.
2. The Committee noted that, due to the small size of the population group being studied, any publications produced need to be very carefully worded to ensure that the participants are not potentially identifiable.

Summary of outstanding ethical issues

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

1. Health information collected in the study needs to be stored for 10 years after the youngest participant turns 16. Please update the protocol and PIS accordingly.

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

1. The second sentence “All patients using C1 inhibitor Berinert® are eligible to participate” implies that other patients are not eligible. Please remove it.
2. The PIS as provided switched between “you” and “your child”. Please make sure that it is consistent throughout.
3. The Committee would like children and adolescents to provide assent. To allow them to do so, please submit age-appropriate assent forms for under 16 year olds (as well as a parent/legal guardian consent form). Note that some of those children may be able to make their own consent, if deemed competent by a medical practitioner.
4. The PIS states “we will also ask you to fill in a questionnaire on your quality of life.” The Committee asked whether the quality of life is of the parents or the child; the Researcher clarified that it is the parent’s perspective of the child’s quality of life. Please amend the PIS to make this clear.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee.
* Please amend the protocol to show that all health information will be retained until 10 years after the last participant finishes the study.

This following information will be reviewed, and a final decision made on the application, by Mrs Sandy Gill and Prof Jean Hay-Smith.

## General business

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

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| --- | --- |
| **Meeting date:** | 13 August 2019 |
| **Meeting venue:** | Sudima Hotel, Christchurch Airport, 550 Memorial Drive, Christchurch |

1. **Problem with Last Minutes**

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

1. **Other business**

It was noted that, due to the change in appointments, Dr Sarah Gunningham would assume the role of Chair going forwards. Ms Raewyn Iodine and Assc Prof Nicola Swain have completed their terms. Two new members, Mr Dominic Flitchett and Dr Pauline Boyles, have joined the Committee as lay members.

The meeting closed at 3:05pm.