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| **Committee:** | Southern Health and Disability Ethics Committee |
| **Meeting date:** | 14 May 2019 |
| **Meeting venue:** | Sudima Hotel, Christchurch Airport, 550 Memorial Drive, Christchurch |

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| **Time** | **Item of business** |
| 11:30 | Welcome |
| 11:35 | Confirmation of minutes of meeting of 09 April 2019. |
| 11:45 | New applications (see over for details) |
| 11:45 – 12:10pm  12:10 – 12:35pm  12:35 – 1:00pm  1:00 – 1:25pm  1:25 – 1:50pm  1:50 – 2:15pm  2:15 – 2:40pm  2:40 – 3:05pm  3:05 – 3:30pm  3:30 – 3:55pm  3:55 – 4:20pm  4:20 – 4:55pm | i 19/STH/81 (Nicola / Jean)  ii 19/STH/87 (Helen / Devonie)  iii 19/STH/86 (Sandy / Nicola)  iv 19/STH/95 (Helen / Paul)  v 19/STH/88 (Jean / Sandy)  vi 19/STH/89 (Helen / Paul) **[COI: Devonie]**  vii 19/STH/90 (Nicola / Jean)  viii 19/STH/91 (Sandy / Nicola)  ix 19/STH/92 (Devonie / Paul)  x 19/STH/93 (Devonie / Paul)  xi 19/STH/94 (Jean / Sandy)  xii 19/STH/82 (Devonie / Helen) |
| 4:55 pm | General business:  Noting section |
| 5:00pm | 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 | Apologies |
| Dr Sarah Gunningham | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | Apologies |
| Assc Prof Nicola Swain | Non-lay (observational studies) | 27/10/2015 | 27/10/2018 | Present |
| Dr Devonie Waaka | Non-lay (intervention studies) | 13/05/2016 | 13/05/2019 | Present |
| Ms Sandy Gill | Lay (consumer/community perspectives) | 30/07/2015 | 30/07/2018 | Present |
| Assc Prof Mira Harrison-Woolrych | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | Apologies |
| Dr Paul Chin | Non-lay (intervention studies) | 27/10/2018 | 27/10/2021 | Present |
| Professor Jean Hay-Smith | Non-lay (health/disability service provision) | 31/10/2018 | 31/10/2021 | Present |
| Mrs Helen Walker | Lay (consumer/community perspectives) | 01/07/2015 | 01/07/2018 | Apologies |

## Welcome

The Chair opened the meeting at 11:30am and welcomed Committee members, noting that apologies had been received from Ms Raewyn Idoine, Dr Sarah Gunningham and Assc Prof Mira Harrison-Woolrych.

The Chair noted that it would be necessary to co-opt members of other HDECs in accordance with the Standard Operating Procedures. Mrs Helen Walker and Ms Sandy Gill of the Central HDEC 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 09 April 2019 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **19/STH/81** |
|  | Title: | Assessing changes to children's lives after fixing their teeth under general anaesthesia. |
|  | Principal Investigator: | Dr Arun Natarajan |
|  | Sponsor: |  |
|  | Clock Start Date: | 11 April 2019 |

Dr Arun Natarajan 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 project is a quantitative study, assessing changes in the Oral health-related Quality of Life (OHRQoL) of children and those living with them after the children have had dental treatment under general anaesthesia. The general functioning of the families of study participants will also be studied.
2. Sociodemographic data will be collected, with socioeconomic status (SES) being determined by parental occupation and categorised using the NZ Socio-economic Index (NZSEI). The household’s street address will also enable an NZDep01 index score to be allocated to each child after geocoding.
3. Three completed questionnaires (one pre-operative and two post-operative at two different intervals (1 month and 4 months afterwards) will be required. These will be completed at the time of regular clinic appointments or follow-up appointments.
4. Statistical analysis will be undertaken in consultation with Prof. W.M. Thomson, University of Otago, Dunedin.

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 the Researcher to provide a brief overview of the study. The Researcher stated they were interested in examining the impact of dental treatment on family functioning and health related quality-of-life for children. The Researcher stated there has not been any in-depth research focused on family functioning and dental treatment.
2. The Committee queried whether the Researcher had access to a translator. The Researcher confirmed they did through the DHB translation service. The Committee queried how the Researcher would approach the questionnaire if a translator was necessary. The Researcher stated it would be done in person with the participant and translator present. The Committee queried whether this would affect the validity of the questionnaire. The Researcher stated it should not and they could go through each question with the translator ahead of time to ensure accuracy. The Committee advised it would be simpler to exclude participants who cannot speak English to preserve the scientific validity of the research but this was up to the Researcher. The Researcher stated they were concerned this could give an inaccurate account of the population. The Committee queried the number of patients attending the clinic who cannot speak English and whether the Researcher had demographic statistics available. The Researcher stated the number varied but was approximately 0 – 2 patients per month. The Committee advised that excluding such few participants would be unlikely to adversely affect the study but acknowledged it was the Researcher’s decision.
3. The Committee queried whether there were other factors that could affect family function over time and if these would be analysed. The Researcher stated they would not track any data that was not captured by the questionnaire. The Committee expressed concern that other external factors could adversely affect family functioning and not be accounted by the research. The Researcher stated it was a validated questionnaire and it made more sense to use a validated one than try to design a custom one. The Researcher explained there was not yet any published research on family functioning and oral health so the study would be a starting point.
4. The Committee queried whether the Researcher would inform the parent’s GP or the child’s GP about participation in the study. The Researcher stated it would be the parent’s GP as they were the participant consenting into the research.
5. The Committee queried how participants would be identified. The Researcher stated potential participants would be identified off the clinic list and an invitation letter would be sent alongside their appointment letter. The Committee queried whether participants would respond to the letter or if they would be approached during their appointment. The Researcher stated the study would be discussed at their appointment. The Committee queried whether the Researcher was part of the regular clinical care team. The Researcher confirmed that they were.
6. The Committee noted the statement on the questionnaire instructing parents not to discuss the questions with the child and queried the harm in participants discussing some of the questions with their child. The Researcher stated there would be little harm but the responses could be variable. The Researcher clarified that they wished to have an answer based on ‘general experience’ rather than the circumstances of the day.

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 whether the questionnaires regarding family functioning could reveal information of concern and how the Researcher would manage responses indicating potential harm. The Researcher stated this was addressed in the cover letter for the application and any concerning issues would be referred to as appropriate. The Committee requested this information be included in the Participant Information Sheet (PIS).
2. The Committee noted the statement that the study would contribute to reducing inequalities between Māori and non-Māori. The Committee queried how the research would do this. The Researcher stated that previous studies have demonstrated there is an inequality between the oral health of Māori and Pākehā and though this study would not directly reduce that it would contribute to a growing body of evidence to prove growing inequality. The Researcher stated a quality improvement audit would then take place in the future. The Committee recommended a generic statement that “inequalities would be examined” rather than framing the research in terms of “Māori versus non-Māori”.
3. The Committee queried the process of Māori consultation and what cultural issues may arise. The Researcher stated they wanted to gain ethics approval before submitting the study for Māori consultation. The Committee advised that they could occur in tandem and requested an update on Māori consultation.
4. The Committee noted the sample size had been increased due to a concern over participants dropping out. The Committee queried what the Researcher expected the drop-out rate to be. The Researcher stated they expected it to be about 10%. The Committee expressed concern that if participants miss an appointment and the research team send them a questionnaire to complete it may deter them from further visits. The Researcher stated they could send text messages to participants to remind them of their appointment to mitigate this risk.
5. The Committee queried the $5 voucher for participation. The Researcher stated it was a token gesture of appreciation for participants’ time. The Committee cautioned that Hospital parking may cost more than that and encouraged the Researcher to increase it to $10. The Committee advised that it was also unclear how frequently the voucher would be given with inconsistent answers in the PIS and application. The Committee requested the Researcher clarify the total amount of vouchers in the PIS.

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

1. The Committee noted the Participant Information Sheet (PIS) uses definitive language and cautioned against over-promising a benefit. The Committee requested more conservative language to reflect that the research is trying to determine *if* the intervention improves family functioning and quality of life.
2. The Committee requested the inclusion of Māori health support contact information in the PIS.

Decision

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

* Please submit an updated Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee.
* Please supply evidence of Māori consultation.

After receipt of the information requested by the Committee, a final decision on the application will be made by Professor Jean Hay-Smith and Assc Prof Nicola Swain.

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| **2** | **Ethics ref:** | **19/STH/87** |
|  | Title: | Tenecteplase in wake-up Ischaemic Stroke Trial (TWIST) |
|  | Principal Investigator: | Dr Teddy WU |
|  | Sponsor: | University Hospital of North Norway |
|  | Clock Start Date: | 02 May 2019 |

Dr Teddy Wu was 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. Tenecteplase in Wake-up Ischaemic Stroke Trial (TWIST) is a randomised-controlled, open-label trial of thrombolytic treatment with tenecteplase for acute ischaemic stroke upon awakening.
2. The trial aims to answer the following questions:

* Can thrombolytic treatment with tenecteplase given within 4.5 hours of wake-up reduce the risk of poor functional outcome at 3 months?
* Can findings on plain CT and CT angiography (and CT perfusion at selected centres) identify patients who benefit from such treatment, compared to patients without such findings?

1. Patients are eligible if they have ischaemic stroke causing measurable neurologic deficits, and can be given tenecteplase within 4.5 hours after awakening. Patients will undergo brain CT and CT angiography (if possible) to exclude large infarction or other contraindications to thrombolytic treatment. Plain CT and CT angiography (if possible) will be repeated on day 2. 500 Patients will be allocated to tenecteplase 0.25 mg/kg as a bolus (maximum dose 25 mg) or to control. The primary effect variable is functional outcome at 3 months, as measured by the modified Rankin Scale (mRS).

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 a brief overview of the study. The Researcher stated the study would allow more people to be treated for an acute stroke. The Researcher stated an agent was used for large clots in Christchurch but not elsewhere in the country. The Researcher explained that the sooner a clot is opened the better for the patient as this could potentially save 90 minutes of brain damage (at a rate of two million neurons a minute). The Researcher stated the primary objective was to show that the intervention was safe and then potentially efficacious.
2. The Committee expressed concern at what appeared to be a consent form for the patient’s family to sign and advised that proxy consent was inconsistent with New Zealand law. The Researcher stated they were aware of this and enrolment would be done by clinician determined best interests consistent with Right 7(4) of the Code of Health and Disability Services Consumers' Rights. The Researcher stated the DHB had a policy whereby it wanted an “agreement form” signed by a family member before the procedure. The Researcher confirmed the form was wholly to satisfy the hospital and was not intended for research participation. The Committee suggested it may be useful to include a statement advising that although the family member has been consulted it is the clinician’s decision whether to proceed.
3. The Committee queried the potential scenario of a family member opposed to the procedure even though the clinician had determined it would be in the individual’s best interest. The Researcher stated this had never occurred in their experience and predicted it to be extremely unlikely as most people understand the sooner a stroke is treated the greater the probability of a successful recovery.
4. The Committee advised that if a participant regained consciousness they could provide consent to participate but only for data going forward. The Committee explained that research undertaken while the participant was unconscious would remain unconsented research. The Researcher confirmed they were aware of this.
5. The Committee queried how a participant indicating severe depression / suicidal ideation in their answers would be managed. The Researcher stated they would make a referral as appropriate or prescribe something personally. The Researcher explained that most stroke patients have community follow-up which includes psychological assessments. Additionally the Researcher stated they would include this information in a letter to the participant’s GP.

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

1. The Committee advised that information regarding pregnancy can be removed from the PIS.
2. The Committee requested the removal of the optional ‘yes / no’ boxes regarding informing the GP and withdrawing data as these are not optional.
3. The Committee requested the inclusion of information on the 90 day questionnaire on the PIS.

Decision

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

* Please amend the Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee.

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| **3** | **Ethics ref:** | **19/STH/86** |
|  | Title: | Scrotal and Core Temperature |
|  | Principal Investigator: | Dr Marilyn Wong |
|  | Sponsor: |  |
|  | Clock Start Date: | 02 May 2019 |

Dr Marilyn Wong 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. Scrotal temperature has been accepted as being 2 to 4oC lower than rectal temperature and 4-6oC lower than body temperature. There are limited human studies conducted specifically comparing normal scrotal and core temperatures despite widespread acceptance of this statement. A higher scrotal temperature has been associated with subfertility in adult men.
2. Primary objective: To qualify the temperature difference statement in the paediatric population by measuring skin, core and scrotal temperatures during elective operations.
3. Secondary objective: Determine temperature differences between patients with inguinal hernia or cryptorchidism and normal patients.

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 a brief overview of the study. The Researcher stated they wished to qualify the statement that the core temperature and scrotal temperature differed as this was commonly cited but there was little conclusive evidence. The Researcher stated studies on subfertility in grown adults measured the temperature but this had not been done in a paediatric population.
2. The Committee queried what clinical value the knowledge would have. The Researcher stated a higher scrotal temperature may affect fertility later as research on subfertility in adults has inferred this link.
3. The Committee queried whether there was any evidence that a higher scrotal temperature as a child would result in subfertility later in life. The Researcher stated it was only theoretical. The Committee expressed concern at informing participants’ parents that they may be sub-fertile without proper evidence. The Committee cautioned that any suspicion of subfertility could not be confirmed until all of the participants mature. The Researcher stated this was not the objective of the study and there was no intention to follow the participants through to adulthood. The Committee queried the objective of the study and its clinical value. The Researcher stated it was observational research to test the commonly accepted temperature difference of 2 – 4°. The Researcher stated other studies cite that number but it is not conclusively established whether the difference range is accurate.
4. The Committee questioned why a paediatric population was necessary and whether the research could be done in adults. The Researcher stated it has not been measured in a paediatric population before and that other studies on adults are mostly studies on infertility. The Researcher stated they just wished to establish whether the temperature difference was accurate or not. The Committee queried whether the research was being done for academic reasons only with no clinical importance. The Researcher stated it was for academic reasons and subsequent studies would be able to cite its findings on temperature.
5. The Committee queried the age range of potential participants. The Researcher stated participants would be 15 years and younger but the majority would likely be presenting with an inguinal hernia so would be infants under 1. The Committee queried whether puberty would affect the validity of the study. The Researcher stated they would be stratifying into ages and analysing whether puberty, adolescent age groups and hormonal changes would have a difference on temperatures. The Committee queried how the Researcher intended to assess how far through puberty a participant was. The Researcher stated there was a staging system and a collaborator could assess this during the procedure. The Researcher stated they had initially intended to simply go by age and thanked the Committee for raising the point.
6. The Committee queried whether the sample size had been designed with stratification in mind. The Researcher stated it had not and 100 was arbitrarily chosen as a round number.
7. The Committee stated the main ethical issue was involving participants in research that would not have value or improve health outcomes. The Committee stated it was difficult to conceive of how the research may improve health outcomes.
8. The Committee advised that health and disability research ought to be undertaken to improve health outcomes, not simply performing research for the sake of doing research.
9. The Committee advised that the study would need a consent form for the older participants to consent to and a range of assent forms for the younger children.
10. The Committee advised that the assent forms need to be child-friendly. Children need to be able to read the form and understand that they can say NO if they do not wish to participate.
11. The Committee advised that several questions in the application form had been answered incorrectly as the study does not involve tissue collection or a low risk medical device.
12. It was not clear whether an oesophageal temperature probe would have been used as standard of care for all cases eligible for study enrolment. The Committee cautioned that using the probe to meet study requirements, where the probe would not have been used by the treating anaesthetist otherwise, adds additional risk that is unlikely to be acceptable given the limited potential benefits of the trial.

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

1. The Committee advised that a large overhaul would be required and recommended the Researcher adapt the HDEC templates:

* <https://ethics.health.govt.nz/system/files/documents/pages/hdec-assent-form-instructions-and-checklist-may18.doc>
* <https://ethics.health.govt.nz/system/files/documents/pages/main-assent-7-11-years-clinical-trial.doc>
* <https://ethics.health.govt.nz/system/files/documents/pages/piscf-template-february-2019-v2.doc>

1. The Committee stated information such as sending tissue samples overseas and information regarding pregnancy was not relevant to the study and could be removed.

Decision

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

* The Committee requested justification for targeting the paediatric population for recruitment and why the study could not be performed in adults. (*Ethical Guidelines for Observational Studies* para 4.8)
* The Committee requested scientific justification on why the study should be performed and what clinical value it may have (*Ethical Guidelines for Observational Studies* para *5.7* )

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| **4** | **Ethics ref:** | **19/STH/95** |
|  | Title: | Maxigesic IV Exposure Study |
|  | Principal Investigator: | Dr. Simon Carson |
|  | Sponsor: | AFT Pharmaceuticals Ltd |
|  | Clock Start Date: | 02 May 2019 |

Dr Simon Carson and Dr Jennifer Zhang 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. A Phase 3, Open-Label, Multiple-Dose, Single-Arm Exposure Study of Maxigesic® IV in Patients with Acute Pain Following Orthopedic, General or Plastic Surgery
2. There is a need that a variety of analgesics through parenteral administration route shall be available where the use of oral analgesics not feasible for post-operative pain relief.
3. AFT developed a fixed dose combination of paracetamol and ibuprofen which is administrated intravenously (Maxigesic IV). In a large phase 3 study, the clinical efficacy and safety of this product has been proven (AFT-MXIV-07) in a post-operative pain model among 275 subjects.
4. During the correspondence with US FDA for New Drug Application, AFT has been required to conduct a large phase 3 safety study to among 225 subjects with at least 50 subjects exposed to the study drug for at least 5 days.
5. This study will be conducted in New Zealand and the USA.

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 a brief overview of the study. The Researcher stated it was an extension of an IV version of pain relief previous shown to be effective. The Researcher stated participants in New Zealand would receive the drug following knee and hip joint replacements. The Researcher stated a larger cohort would receive the drug in the USA. The Committee stated this information had not been included with the application which makes it difficult to assess.
2. The Committee noted the study would require at least 150 patients to have a 95% chance of picking up a single case of TAE that is only expected to have an incidence of 2%. The Committee queried whether the study numbers would be adequate. The Researcher stated the data would complement the larger study in the USA and confirmed the data would be combined.
3. The Committee stated there were numerous issues with the application form with many questions answered incorrectly.
4. The Committee queried the response to question B.4.1 which stated data would not be made available to regulatory authorities. The Researcher apologised for the error and stated data from the trial would be submitted to the FDA.
5. The Committee noted the response to section 4.4 on termination of the study discussed withdrawing individuals and not halting the study. The Committee queried whether there were study specific protocols for terminating the entire study. The Researcher confirmed there were and the study could be halted for safety reasons.
6. The Committee queried how potential participants would be identified if health information would not be screened. The Researchers stated two privately-practicing orthopaedic surgeons would identify suitable patients and ask if they are interested in the study and if so their details would be provided to the study team. The Researcher confirmed only a named investigator would manage the informed consent process.
7. The Committee noted the incomplete response to question R.2.3 regarding participant confidentiality. The Committee queried how confidentiality of health information would be ensured. The Researcher stated they would keep their own source documents which only staff could view. The Researcher stated some information would be copied from the participant’s hospital record but it would only be passed on de-identified.

The Committee queried how long records would be retained. The Researcher stated at least 15 years but likely longer as it will be stored electronically.

1. The Committee queried how incidental findings of blood tests / ECG would be managed. The Researcher stated the participant would be notified. The Researcher stated if the incidental finding would affect the surgery the surgeon and anaesthetist would be informed or if it was otherwise significant they would contact the participant’s GP personally.
2. The Committee queried whether locality approval would be sought from St. George’s. The Researcher confirmed it would.

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 whether participants would have access to non-pain relief drugs if necessary. The Researcher confirmed they would with only paracetamol and ibuprofen forbidden.
2. The Committee noted the PIS states participants may have to halt all drugs, herbal supplements etc. The Committee requested the Researcher amend this to state only paracetamol and ibuprofen cannot be taken

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1. The Committee queried whether the source collection forms would be identifiable. The Researcher stated they did require ID from participants to confirm their identity which would be recorded in the source document. The Committee explained this meant the source document was identifiable information and requested the Researcher state this in the PIS.
2. The Committee requested the inclusion of a cultural statement. The Researcher stated they were waiting for ethics approval before submitting the study to the Māori cultural advisor. The Committee requested an update.
3. The Committee advised the correct article of the treaty is 3 and not 2. The Committee advised that for future applications it would be helpful to include information on the prevalence of the health condition in Māori supported by statistics and whether the research may benefit Māori rather than a dubious reference to the Treaty of Waitangi.
4. The Committee noted authoritative language in PIS (“..we will inform your GP, we will contact X..”. The Committee explained that these things happen with participants’ consent as indicated by the optional “yes / no” boxes on the consent form. The Committee requested the tone of language in the PIS is revised to reflect that these are optional. Alternatively if they are mandatory then remove the “yes / no” boxes from the consent form.
5. The Committee cautioned against over-promising the intervention and that it will be effective pain relief after surgery. The Committee stated that although it is the Researcher’s belief that the intervention will help they cannot bias the results by telling participants that it will be effective. The Committee requested a revision in the PIS to use more conservative language and to state that the study will determine *if* the intervention is effective.
6. The Committee noted that question R.3.1 on the use of human tissue had been answered incorrectly and as a result subsequent important questions regarding human tissue were not answered. The Committee requested the Researcher answer these questions on resubmission in order to provide the required information regarding testing and disposal of human tissue.

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

1. The Committee stated the entire PIS needs a thorough revision and suggested the Researcher adapt the HDEC template:

<https://ethics.health.govt.nz/system/files/documents/pages/piscf-template-february-2019-v2.doc>

1. The Committee noted the Participant Information Sheet (PIS) says participants will be required to spend 2 – 5 days at the study site and queried what this is. The Researcher stated it should read ‘hospital’ and clarified the study site was the hospital participants are recruited in as well as the research clinic. The Committee requested the Researcher amend the form to state the site is St George’s Hospital with the follow-up at Southern Clinical Trials.
2. The Committee stated it was not clear from the PIS that the stay was 48 hours and requested a revision for clarity.
3. The Committee requested the ‘introduction’ section be placed at the beginning of the PIS.
4. The Committee requested the references to “parents / legal guardians” are removed as this is not appropriate for a New Zealand context.
5. The Committee noted the ACC statement was outdated and requested the Researcher use the new wording available on the HDEC template.
6. The Committee requested the inclusion of information regarding reproductive risks.
7. The Committee advised that the translator statement is not required.
8. The Committee noted reference to “agents” reviewing medical records but the sheet does not state for what purpose. The Committee advised that the sponsor should not have access to identifiable information unless it is the on-site monitor. The Committee requested a revision to the confidentiality section.

Decision

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

* Please address how the study may benefit Māori and how cultural issues that may arise for Māori participants in the study will be managed (*Ethical Guidelines for Intervention Studies* paragraph4.7).
* Please supply a Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee. (*Ethical Guidelines for Intervention Studies* paragraph6.22).
* Please ensure all answers in the application form are answered correctly to allow the Committee to properly assess the application. (*Standard Operating Procedures for Health and Disability Ethics Committees* para)

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| **5** | **Ethics ref:** | **19/STH/88** |
|  | Title: | An investigation into the clinical significance of Arcobacter species in New Zealand. |
|  | Principal Investigator: | Miss Casey O'Byrne |
|  | Sponsor: | Massey University |
|  | Clock Start Date: | 02 May 2019 |

Miss Casey O’Byrne 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 research aims to provide information about the prevalence and distribution of the potential foodborne bacterial pathogens Arcobacter butzleri, Arcobacter cryaerophilus, and Arcobacter skirrowii isolated from clinical specimens in the lower North Island of New Zealand. The data collected may be used to determine the clinical significance of such isolates and as such, whether they should be included in routine Medical Laboratory testing for the investigation of enteritis.
2. The initial collection and processing of samples collected from the; Wellington, Hutt Valley, and Wairarapa regions will be performed at the Medical Laboratory in Masterton. An estimated 2,500 patient stool samples sent to the participating Laboratories for faecal pathogen screening will have additional testing for Arcobacter species conducted over a period of approximately three months, after all routine testing is complete. Based on previous studies, an estimated 25-30 suspected Arcobacter species will be isolated from this initial enrichment process. Suspected Arcobacter isolates will be identified to the species level and analysed using Polymerase Chain Reaction (PCR) sequencing at Massey University. The antimicrobial susceptibility patterns of the confirmed Arcobacter species will be measured to form a comparison with international populations.
3. Relevant information such as the detection of other faecal pathogens by multiplex PCR and some demographic information including the patients region (Wairarapa, Hutt Valley, or Wellington) and gender would also be recorded to establish a pattern of prevalence.

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 the results of the study and presence of arcobacter in samples had the potential to affect the clinical management of participants. The Researcher stated they would not. The Researcher explained that it has not yet been determined if the organisms cause diarrhoea as it is difficult to prove a causative link. The Researcher stated the study may contribute to this long process if a strong correlation were found with no other pathogens present.
2. The Committee queried the timeframe of the study and when samples would be analysed. The Researcher stated samples would be isolated, frozen and then compared concurrently. The Researcher explained this would likely be months after the sample was produced and any clinical symptoms would likely have passed.
3. The Committee queried if there were any clinical reasons to add the presence of the organism to an individual’s medical records. The Researcher stated not at this stage as not enough about the organism was known to definitively classify it as a pathogen.
4. The Committee queried whether use of the samples fell under a different purpose for which they were provided. The Researcher stated yes and no as they were provided to the lab for a faecal PCR (polymerase chain reaction) test and that the research would submit the sample for an additional PCR. The Committee was satisfied the additional test was not an unreasonable secondary use.
5. The Committee queried the identifiability of the samples. The Researcher stated they would be labelled with the lab ID number but this would not be used for the research and instead a unique study ID code would be assigned.
6. The Committee queried the answer to question P.4.3 in the application where the Researcher had stated Māori consultation was not required. The Committee advised that any research that may potentially involve Māori participants (or their tissue) must undergo a consultation process. The Researcher stated the lab has procedures to return specimens to patients if they wish and these samples would be diverted before reaching the disposal area. The Researcher stated they did not anticipate the use of these being an issue as the samples would otherwise have been destroyed. The Committee explained as Māori tissue would potentially be used in the research a formal consultation process is still required. The Researcher agreed to this and queried whether it should come through CCDHB or Massey University. The Committee stated either would suffice and to use whichever the Researcher found most appropriate.

Decision

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

* Please undertake formal Māori consultation prior to commencing the study.

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| **6** | **Ethics ref:** | **19/STH/89** |
|  | Title: | GS-US-402-4374: A study comparing how fast the trial drugs GS-9674 and GS-0976 are cleared from the body, in healthy adults and in adults with severely reduced kidney function. |
|  | Principal Investigator: | Dr Richard Robson |
|  | Sponsor: | Gilead Sciences, Australia and New Zealand |
|  | Clock Start Date: | 02 May 2019 |

Dr Richard Robson was 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.

Dr Devonie Waaka declared a potential conflict of interest and the Committee agreed to allow the member to remain in the room but would not contribute to the discussion or take part in the decision.

Summary of Study

1. GS-0976 and GS-9674 which are being developed for the treatment of Nonalcoholic Steatohepatitis (NASH), a disease in which the liver becomes fatty and enlarged and may not work properly.
2. The kidneys play a minor role in clearing GS-9674 and GS-0976 from the body, so reduced kidney function should not result in a build-up of either study drug in the blood. The study team wants to confirm this by comparing levels of the study drugs in blood and urine following single doses, in adults with severely reduced kidney function and in adults whose kidneys are working normally.
3. Two groups will be enrolled in the study:

* Group 1: approximately 10 adults with severely reduced kidney function, and
* Group 2: approximately 10 adults with normal kidney function.

1. Each participant in Group 2 will be selected as a 'match' for a Group 1 participant, based on age, body mass index (BMI) and gender.
2. Every person in the study will receive:

* - a single 20 mg oral dose of GS-0976 on Day 1
* - a single oral dose of GS-9674 placebo on Day 6
* - a single 100 mg oral dose of GS-9674 on Day 7

1. Levels of the study drugs will be measured in blood and urine samples collected at specific times after dosing. Safety assessments will be performed, biomarker samples will be collected, and any changes in health will be recorded.
2. The results will provide important information about whether the doses of GS-0976 and GS-9674 can remain unchanged when used by patients with reduced kidney function.

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 the Researcher to provide a brief overview of the study. The Researcher explained the study would be looking at two medicines developed to treat fatty liver disease, commonly caused by excess alcohol or weight related diabetes. The Researcher stated the drugs have both been developed to treat steatohepatitis but have a slightly different mechanism. The Researcher explained for regulatory purposes they would need to determine whether renal function affected the disposition of the drugs. The Researcher predicted that it would be a long study and difficult to recruit as it require a lengthy time commitment from participants.
2. The Committee queried what the study would involve for participants. The Researcher stated they would come into the clinic and take the medication, have blood and urine samples collected followed by a wash out period with placebo tablets. The Researcher stated they would stay in the clinic for 11 days then return home. The Researcher confirmed there would be follow up tests afterward.
3. The Committee queried the risks involved for the study. The Researcher stated some minor risks were identified on the Participant Information Sheet (PIS). The Researcher stated they did not expect it to be a high-risk study as participants would only receive a single dose of the drug. The Researcher acknowledged that as it is a new medicine there is some uncertainty so they cannot definitively state there is little to no risk.
4. The Committee queried whether the pharmacokinetics would analyse the total or unbound drug. The Researcher stated they would examine the total amount.

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 Future Unspecified Research (FUR) involving genetic testing and stated the PIS could include more information on what may be tested and why. The Researcher stated as FUR is unspecified they could not predict what it may involve in the future but would be interested in how genes may affect fatty liver disease.
2. The Committee requested the Researcher split the PIS into the main study and create a separate optional form for the FUR. The Committee recommended the Researcher adapt the FUR template available on the HDEC website:

<https://ethics.health.govt.nz/system/files/documents/pages/fur_piscf_template.doc>

1. The Committee queried whether in the event of a participant or male participant’s partner becoming pregnant the Researchers would want to collect information on the pregnancy. The Researcher stated they would. The Committee advised that this would require a separate form for the pregnant woman to complete and an additional consent process to collect information on the child after the birth.

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

1. The Committee identified a typo in the PIS stating participants would be reimbursed $36,400. The Researcher confirmed this was an error and the amount should be $6,400.
2. The Committee requested the addition of a clear heading for the optional future research and genetic addendum in the main PIS.
3. The Committee requested the inclusion of additional information regarding the optional future unspecified research in the addendum.

Decision

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

* Please supply an updated Participant Information Sheet and Consent Form, taking into account suggestions made by the Committee.

After receipt of the information requested by the Committee, a final decision on the application will be made by Mrs Helen Walker and Dr Paul Chin.

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| **7** | **Ethics ref:** | **19/STH/90** |
|  | Title: | CA017-078 |
|  | Principal Investigator: | Dr Peter Fong |
|  | Sponsor: | Bristol-Myers Squibb |
|  | Clock Start Date: | 02 May 2019 |

Dr Peter Fong and Pallavi Wyawahare 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. The purpose of this research project is to assess the safety, effectiveness and tolerability of the experimental treatment, BMS-986205 in combination with nivolumab and chemotherapy (gemcitabine + cisplatin), before and after surgery.
2. The effectiveness of this experimental treatment will be compared with (1)a placebo in combination with nivolumab and chemotherapy, and (2) chemotherapy (gemcitabine + cisplatin) given alone, in participants with muscle-invasive bladder cancer.
3. Participants will undergo a number of procedures at different time points to determine if they have responded to treatment.

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 necessity of treatment arm B needing a placebo. The Researcher stated this was because there was no indication that maintenance therapy after surgery provides a definitive benefit. The researcher stated there was equipoise in this regard as it is unknown whether it could help or risk further side effects unnecessarily.
2. The Committee noted the Participant Information Sheet (PIS) was very dense. The Researcher stated they did not have much input into its design as it was a large multisite international study.
3. The Committee queried why four options for radiation were listed on the PIS (page 17). The Researcher stated this was an error and only one option (the third) would be kept to inform participants of the radiation exposure due to participation.
4. The Committee queried whether the optional biopsy would be a cystoscopy and if participants would be aware of this invasive procedure. The Researcher confirmed it would be a cystoscopy and stated participants would have already received multiple cystoscopies so would be familiar with the procedure. The Researcher confirmed they would be informed during the consent process for the optional biopsy.
5. The Committee noted the application’s response to question R.1.3 which stated standard treatment would be withheld. The Committee queried what treatment would be withheld as it could not identify any information regarding this on the Participant Information Sheet (PIS). The Researcher stated standard treatment for advanced bladder cancer was chemotherapy (if the patient was well enough to have it) and that any participants not well enough for chemotherapy could not be in the study. The Researcher confirmed no standard treatment was being withheld and the answer in the application form was an error. The Researcher apologised for this oversight.

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 Researcher’s plan for disseminating results of the study to the participants. The Researcher stated the participants would continue to receive follow-up appointments in the long term and they intended to inform them verbally (or over the phone if they could not come into the clinic). The Researcher stated it was difficult to predict when the results of the study would be available as this would depend on the rate of recruitment. The Committee requested the inclusion of an option to receive a copy of the study results with a “yes / no” box on the consent form.
2. The Committee queried the response to question P.2.7 regarding if information is discovered of relevance to continued participation. The Committee noted the response said the form would be submitted to HDEC for approval and then participants would be informed afterward. The Committee advised this process was the wrong way around and that if something is of a concern that it may impact participants’ desire to remain in the study it would expect participants are informed before documentation is submitted for HDEC review, especially in regard to safety information. The Researcher agreed that participant safety was of paramount importance and stated they would not wait for a follow-up. The Researcher confirmed that information of concern would be acted upon immediately rather than waiting for the next clinical visit, or for HDEC approval of an updated PIS/CF.
3. The Committee advised that the PIS for pregnant participants needs an amendment as the baby cannot be consented until after birth. The Committee explained the pregnant women can sign for herself during the pregnancy but the baby only becomes a legal entity upon birth.
4. The Committee advised that verbal withdrawal is permitted in New Zealand and the onus is on study staff to perform the paperwork. Participants are not required to sign anything to withdraw.
5. The Committee advised that for future applications it would be helpful to include information on the prevalence of the disease in Māori supported by statistics and whether the research may benefit Māori rather than a dubious reference to the Treaty of Waitangi

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

1. The Committee noted the clause in the PIS granting third parties extensive access to participant records. The Committee reasoned that although it would likely only be used for monitoring and audit purposes the statement was nevertheless a *carte blanche* for unlimited access by the Sponsor. The Researcher stated as a registration study a regulatory authority may audit the study and its records. The Committee advised that a statement informing participants of that would be sufficient and granting broad open access was unnecessary. The Committee requested the Researcher amend the clause in the main PIS and future unspecified research form to state records may be audited by a regulatory authority.
2. The Committee queried if data on pregnant participants / their babies would be sent overseas. The Researcher stated it would but would be partially de-identified. The Committee requested the inclusion of information regarding this to the pregnant partner PIS.
3. The Committee requested the inclusion of advocacy contact details, Māori health contact details and the Health and Disability Commissioner contact details on the pregnant partner PIS.

Decision

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

* Please provide an updated Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee.

After receipt of the information requested by the Committee, a final decision on the application will be made by Professor Jean Hay-Smith and Assc Prof Nicola Swain.

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| **8** | **Ethics ref:** | **19/STH/91** |
|  | Title: | Microdosing LSD |
|  | Principal Investigator: | AP Suresh Muthukumaraswamy |
|  | Sponsor: | The University of Auckland |
|  | Clock Start Date: | 02 May 2019 |

Associate Professor Suresh Muthukamaraswamy and Dr Nicholas Hoeh 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. The study is a randomised, double-blind, placebo-controlled crossover trial of repeated microdoses of LSD in healthy volunteers.
2. “Microdosing” refers to repeated administration of psychedelics such as LSD or psilocybin in doses below the threshold for overtly altering perception. There is a growing microdosing subculture and grey literature suggesting that this practice can enhance creativity and productivity, improve mood and favourably modify personality traits. These claimed effects are similar to those observed in clinical studies, in which participants receive much larger, perception-altering doses of LSD or psilocybin. However, there are as yet no controlled, scientific studies of the psychological or physiological effects of repeated psychedelic home-self-administered microdosing.
3. Given the powerful nature of placebo and expectancy effects on self-reports, controlled trials are required to objectively evaluate the effects of microdoses of psychedelic drugs in humans. In this study, the research team aims to conduct a randomised controlled trial of repeated microdoses of LSD under schedules similar to those suggested in the grey literature.
4. 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.
5. 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.
6. The results will tenable a more rigorous evaluation of the purported benefits of psychedelic microdosing and will be relevant to the question of whether microdosing may be a viable alternative treatment regimen for depression or addiction.

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 a brief overview of the study. The Researcher stated there was popular media attention on microdosing psychedelic drugs and the claims that these small doses (1/10 a regular dose) have positive effects. The Committee queried whether microdoses of LSD has been studied before. The Researcher stated not in a well-controlled environment and that much of the data is anecdotal.
2. The Committee queried whether the study required approval by SCOTT. The Researcher confirmed this was underway but they were awaiting information on technical formulation questions in order to proceed.
3. The Committee queried whether Māori were excluded from the research. The Researchers stated they were not. The Committee queried whether Māori consultation for the study had been undertaken. The Researchers confirmed this was in progress.
4. The Committee queried how the research may benefit Māori. The Researchers stated they had submitted the study to the DHB for Māori consultation. The Committee queried the Researchers views. The Researchers stated there may be Māori participants but the small sample size would not allow them to do separate demographic analysis. The Researchers stated it would be difficult to predict whether there would be any specific benefit to Māori beyond the generic knowledge gain.
5. The Committee queried whether the conditions the Researchers were intending to treat affected Māori equally. The Researchers stated they would not be treating any conditions in this study. The Committee queried the study’s hypothesis and potential health benefit of the research. The Researchers stated they did not know for certain whether there will be a health benefit. The Researchers stated their objective was to test the anecdotal claims that microdosing LSD may provide benefits to personality, cognition and feelings of wellbeing.
6. The Committee queried whether microdosing could potentially be used for health benefit in the long term. The Researchers stated if a positive effect was demonstrated it may be able to be used in some kind of indication. The Researchers stated the study was primarily concerned with evaluating the international anecdotal claims of benefit and to explore the validity of these claims. The Researchers stated the opposite may be true and they may discover that microdosing is harmful or detrimental. The Researchers stated it is difficult to anticipate the outcome as it could go in either direction. The Researchers stated if the study demonstrated a benefit this could provide a foundation for future research into extending it toward treating mental health or alternatively if harm was demonstrated this could disseminated to the general population so individuals are aware of the risks.
7. The Committee queried the genetic analysis to be undertaken. The Researcher stated there was not much data on how pharmacokinetic factors may change in response to the drug and so some of the key genotypes in terms of drug disposition were selected. The Committee queried whether the small number of participants would allow the Researcher to come to any useful conclusions. The Researcher stated it was intended as a secondary objective to gather pilot data.
8. The Committee queried the source of funding from the study. The Researcher stated it was a philanthropic donation. The Committee queried whether the funder had any involvement in the design of the study. The Researcher stated they did not. The Researcher explained they were providing funding only and no input on the design or conduct of the study. The Committee queried whether the funder had any financial interests in the outcome of the study either way. The Researcher confirmed they did not.
9. The Committee queried whether there were any restrictions on publication. The Researcher stated in order to receive the drug they would have to receive confidential intellectual property, which the donor/funder wanted to ensure did not appear in any publication resulting from this study. The Researcher stated they were still finalising the contract but the supplier of the drug could request a 60 day delay to ensure the intellectual property is not in any publication.
10. The Committee noted the claim that microdosing may be beneficial for mood and queried whether the Researcher was planning to measure the mood of participants. The Researcher stated participants would perform nightly mood scales on their phone and would complete a more thorough assessment at clinical visits.
11. The Committee queried the safety monitoring plan for the event of a participant indicating severe distress or suicidal ideation. The Researchers stated participants should contact the study team for anything major. The Committee queried how participants would know what is major. The Researchers stated participants would have to use their own judgement but if anything was of concern to them then they should contact the research team. The Committee queried whether the nightly mood scales had a ‘cut off’ point to suggest action should be taken. The Researchers stated they did not as they were not that sensitive.
12. The Committee queried the risks of self-administering LSD and why the dosing would not be done under direct observation at the clinic. The Researchers stated part of the ‘ecology’ of the anecdotal claims was that the microdosing took place at home. The Researchers stated this would be important for the environmental stimulus to examine the claim of microdosing modifying neuroplasticity.
13. The Committee queried how participants coming into the clinic to take the dose before returning home would be invalidating. The Researchers stated that would involve 28 trips into the clinic in central Auckland and may be an undue burden on participants.
14. The Committee raised the concern with outpatient dosing of participants hoarding doses to either combine doses or share with others. The Researchers stated they had given this consideration and it would be a major deviation from protocol. The Researchers stated joining the trial to abuse the dosing would involve a lot of effort compared with the relative ease of illicitly buying LSD on the black market. The Committee cautioned volunteers may be enticed into joining the study in order to access a controlled drug. The Researchers stated the participants would be required to fill out the nightly surveys and if any were misbehaving they would be unlikely to comply with this so would be removed from the study. The Researchers stated participants would only receive 4 or 5 doses at a time. The Committee expressed concern that participants could be deceitful and would still have the ability to stockpile doses. The Committee also noted that observed dosing allowed closer assessment of participants in terms of adverse event monitoring and participant safety. The Committee recommended the dosing take place in clinic and requested the Researcher provide a justification for the outpatient dosing plan.
15. The Committee noted the six monthly schedule for the Data Safety Monitoring Committee to meet and queried the duration of the study. The Researcher stated they expected it would between one and two years. The Researchers stated with a schedule of procedures involving 240 visits they expected it would be a long study.
16. The Committee noted inconsistency with the placebo tablet being referred to as an inactive tablet but also described as containing caffeine. The Researcher stated this was an error from a previous version and apologised. The Researcher confirmed the placebo tablet would be inactive.
17. The Committee queried whether microdosing LSD carried any reproductive risks. The Researchers stated there was limited evidence that LSD had any reproductive risk. The Researchers stated only males will be enrolled on the trial. The Committee queried whether there was evidence of transmission of LSD through semen. The Researchers stated there was not.
18. The Committee queried the qualitative aspect of the research involving participants uploading a video from their mobile phone. The Researcher stated it would depend on the phone’s capabilities but they were only interested in the audio recording, not the video. The Committee queried whether the recordings would be transcribed. The Researchers confirmed it would. The Committee queried whether the audio recordings would be deleted after transcription. The Researchers stated they would not as they may be useful to review. The Committee requested this be clearly stated in the Participant Information Sheet.
19. The Committee queried whether the transcriber of the audio recordings would maintain confidentiality. The Researchers confirmed they would need to sign a confidentiality agreement. The Researchers stated they would set up a VPN and did not expect the data to leave their servers.
20. The Committee queried whether ACC would be applicable for a trial involving a class-A drug and requested the Researchers investigate this.
21. The Committee queried the media interest in the study. The Researchers explained staff from Newshub were interested in creating a documentary and potentially filming some of the participants. The Committee queried how the confidentiality of participants who refuse to be filmed would be protected. The Researchers stated only one participant will be at the unit at a time so the film crew would not be invited on the days the participant had not consented.
22. The Committee noted risks listed in the investigator’s brochure were not listed in the PIS (e.g. headache). The Committee advised that any potential adverse effects no matter how improbable must be included in the PIS so participants are fully informed.
23. The Committee noted some of the assessment tools were specialised and queried whether they would be performed by someone properly qualified. The Researchers stated Dr Nicholas Hoeh, consultant psychiatrist will perform them or if he is not available another similarly qualified investigator. The Researchers stated they want to emphasise healthy control for screening and recruiting.
24. The Committee stated it was possible that LSD even in limited doses may impact some people more than others. The Researchers acknowledged this and stated it has not been studied rigorously recently. The Researchers stated many of the studies from the 1960s were not very robust and it was difficult to compare them to the anecdotal experiences from today.
25. The Committee queried the time frame of the audio recordings from upload to transcription. The Researchers stated there would be a long time in between. The Committee queried how the Researchers would recognise any psychosis participants may be experiencing from home dosing. The Researchers stated participants would be provided with a card of contact details for use in an emergency. The Committee expressed concern that an individual who may not be thinking clearly may not remember they have the card. The Researchers suggested that the study team could contact a participant who had not completed their questionnaire for a day or two.
26. The Committee queried whether this would be appropriate for a high risk drug. The Researchers stated they were very low doses and there was no evidence of low doses triggering a psychiatric episode. The Researchers cited studies that showed no discernible psychological effect at 10μg over placebo. The Researchers suggested they could implement more safety checkpoints such as a follow-up call on microdosing days. The Committee agreed this was a good idea as the Researchers could not guarantee the emotional or mental state of participants. The Researchers stated this would involve 26 calls per participant and queried whether a text message would suffice. The Committee responded that this may potentially be acceptable, provided the Researchers ensured they received a response to each text.
27. The Committee queried whether the Researchers could legally supply the drug to participants. The Researchers stated Medsafe allows up to four weeks of a class-A drug to be prescribed to an individual. The Committee reasoned that a prescription for treatment was different to supply for a clinical study. The Committee raised the scenario of a participant receiving the study dose then being stopped and searched by police on the way home. The Committee requested the Researcher provide a legal opinion stating that the trial as proposed would be acceptable under New Zealand law. The Committee recommended the Researchers consult with the University regarding this process.

Decision

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

* Please supply an updated Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee.
* Please provide a strong justification for an out-patient dosing regime, addressing all the concerns raised by the Committee.
* Please submit evidence of SCOTT approval.
* Please supply the summary of a legal opinion confirming that providing a Class-A drug to participants in the community would not violate any laws of New Zealand to ensure legal protection for participants.
* Please confirm whether study participants would be eligible for ACC in the event of an accident.

After receipt of the information requested by the Committee, a final decision on the application will be made by the full Southern HDEC Committee at the next available meeting.

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| **9** | **Ethics ref:** | **19/STH/92** |
|  | Title: | Food-Effect Study of 12 mg Tretinoin capsules in Healthy Male Subjects. |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Douglas Pharmaceuticals Ltd |
|  | Clock Start Date: | 02 May 2019 |

Dr Noelyn Hung was not present for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The study This study is comparing how the tretinoin is absorbed, distributed and eliminated in your body both with and without the presence of food. Tretinoin is a known teratogen so only males are participating in this study.
2. Two single doses of tretinoin will be administered to the participants in fed (one dose) and fasted states (one dose).
3. Subjects will be recruited within 3 weeks (21 days) prior to the study commencing. Fifteen (15) days will be required for sample collection. There will be at least 2 weeks washout between each dosing period.
4. Subjects will be housed at the Zenith Clinical Site 12 hours before dosing until all clinical procedures have been completed (12 hours after dosing).
5. Blood samples will be collected at baseline and at specified times up to 12 hours after dosing. The plasma will be assayed for tretinoin only using a fully validated LC-MS/MS method.
6. To assure the good health of subjects, pre-study physical examinations, vital signs, ECG and clinical laboratory tests will be performed. Post-study laboratory tests will also be carried out and subjects will be monitored for AEs throughout the study.

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 charter for the independent data safety monitoring committee and requested details of who it will comprise of and the conditions under which a meeting would be triggered.

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

1. The Committee requested the inclusion of an optional “yes / no” box for participants to indicate that they wish to receive a summary of the results of the study.
2. The Committee advised that the risks sections needs to include all of the less common side effects. The Committee requested this be updated with all the risks listed in the product brochure.
3. The Committee noted the absence of information regarding reproductive risk. The Committee requested the Researcher adapt the section available on the HDEC template and adjust as appropriate for the study.

Decision

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

* Please supply details of the IDSMC.
* Please supply an updated Participant Information Sheet with the information requested by the Committee.

Please submit the above through the HDEC amendment pathway.

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| **10** | **Ethics ref:** | **19/STH/93** |
|  | Title: | Comparison of Tretinoin capsules in Healthy Male Subjects. |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Douglas Pharmaceuticals Ltd |
|  | Clock Start Date: | 02 May 2019 |

Dr Noelyn Hung was not present for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. T This study is comparing how the tretinoin is absorbed, distributed and eliminated after taking both a 12 mg and 10 mg formulation on two separate occasions. Tretinoin is a known teratogen so only males are participating in this study.
2. During each treatment period, the enrolled and randomised healthy male subjects will receive a single dose of 1 x 12 mg tretinoin capsule or a single dose of 1 x 10 mg tretinoin capsule under fed conditions.
3. Subjects will be recruited within 3 weeks (21 days) prior to the study commencing. Fifteen (15) days will be required for sample collection. There will be at least 2 weeks washout between each dosing period.
4. Subjects will be housed at the Zenith Clinical Site 12 hours before dosing until all clinical procedures have been completed (12 hours after dosing).
5. Blood samples will be collected at baseline and at specified times up to 12 hours after dosing. The plasma will be assayed for tretinoin only using a fully validated LC-MS/MS method.
6. To assure the good health of subjects, pre-study physical examinations, vital signs, ECG and clinical laboratory tests will be performed. Post-study laboratory tests will also be carried out and subjects will be monitored for AEs throughout the study.

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

1. The Committee queried the charter for the independent data safety monitoring committee and requested details of who it will comprise of and the conditions under which a meeting would be triggered.

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

1. The Committee requested the inclusion of an optional “yes / no” box for participants to indicate that they wish to receive a summary of the results of the study.
2. The Committee advised that the risks sections needs to include all of the less common side effects. The Committee requested this be updated with all the risks listed in the product brochure.
3. The Committee noted the absence of information regarding reproductive risk. The Committee requested the Researcher adapt the section available on the HDEC template and adjust as appropriate for the study.

Decision

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

* Please supply details of the IDSMC.
* Please supply an updated Participant Information Sheet with the information requested by the Committee.

Please submit the above through the HDEC amendment pathway.

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| **11** | **Ethics ref:** | **19/STH/94** |
|  | Title: | External Stimulators To Augment Rehabilitation Therapy (ESTART trial) |
|  | Principal Investigator: | Associate Professor John Reynolds |
|  | Sponsor: |  |
|  | Clock Start Date: | 02 May 2019 |

Professor John Reynolds 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 investigates the use of an external stimulator for use during rehabilitation following stroke.
2. After stroke, 85% of patients never regain full function in the arm and hand. This accounts for much of the poor feelings of well-being that follows stroke. Recovery from stroke requires that nerve cells in adjacent brain areas take over some of the lost function. However, this is thought to be difficult to achieve in brain areas around a stroke because of an increase in the activity of circuits that tend to ‘turn off’ or ‘inhibit’ these areas.
3. One of these circuits originates in the motor cortex in the opposite side of the brain to that affected by the stroke. The Researchers intend to alter the activity of this circuit using a treatment called neuromodulation, allowing greater gains to be achieved by concurrent rehabilitation.
4. In the proposed human feasibility and safety study, which is based on experimental neuroscience reported in rat models and a pilot study using implanted electrodes in two humans the study will investigate a novel approach to modulating this inhibition using external electrical stimulation delivering bursts of electrical pulses to the motor cortex on the opposite hemisphere from the stroke.
5. This will be combined with a physiotherapy programme designed to maximize the improvement in functioning of the affected arm and hand.

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 the Researcher provide a brief overview of the study. The Researcher stated a previous study with invasive stimulators had two participants that responded well, one subsequently died a year later of natural causes and the second is still doing well. The Researcher explained the stimulator in that study was invasive and so they did not recruit as well as they had hoped. The Researcher stated the non-invasive stimulator may appeal to potential participants put off by the previous study.
2. The Committee queried whether the device improves rehabilitation following stroke. The Researcher stated they needed to be cautious as the new device is different to the previous one. The Researcher stated they could not guarantee an improvement because the study is primarily about the safety and feasibility of the device rather than a measure of its efficacy.
3. The Committee advised the PIS could be potentially confusing to a participant as it was unclear on the schedule when active stimulation versus sham therapy was being administered. The Researcher stated it was deliberately vague as they did not want the participants (or therapists) to know there was no stimulation turned on during the first three weeks. The Researcher explained they wanted to maximise improvements through rehabilitation alone and by telling participants / therapists it was not turned on this may bias results and harm the scientific validity of the study. The Researcher agreed to revise the section. The Committee suggested the Researcher could adapt the following paragraph:

*“…every participant will receive active stimulation for X weeks and active stimulation and sham stimulation for Y weeks. Participants, doctors and physiotherapists will not know which period of time the stimulator will be active for (but this can be revealed in the event of an emergency).”*

1. The Committee queried whether all the physio assessments of function would be hand and arm function. The Researcher confirmed it would. The Committee suggested the Researcher could include additional information on the tests (e.g. ‘brush hair’ or ‘hold arm above head’ etc) in the PIS so participants understand what will be expected of them.
2. The Committee advised that an open-label follow-up would require the submission of an amendment or new application to carry the study over.
3. The Committee recommended separating the Participant Information Sheet (PIS) into two versions, one for healthy volunteer participants and one for patient participants. The Committee reasoned the PIS contained a lot of information regarding procedures the healthy participants will not require.

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

1. The Committee queried whether enrolment in the study would affect any community rehabilitation participants may be receiving. The Researcher stated if any potential participants were receiving active rehabilitation that would not necessarily be an exclusion but would be discussed during enrolment. The Committee requested this be made clear on the Participant Information Sheet (PIS).
2. The Committee queried what would interaction participants would have in between the 12 weeks of therapy and 6 month follow up and noted this was not clear by reading the PIS. The Researcher stated after the 12 weeks had finished the participant will be set up with a home programme and then not seen for six months. The Committee requested this be clearly stated in the PIS.
3. The Committee noted the information contained in the protocol was minimal. The Committee advised that another research team ought to be able to faithfully replicate the study from the protocol alone and requested the Researcher revise and expand it.
4. The Committee requested more information regarding participant safety and risks is added to the PIS and protocol.
5. The Committee noted the Māori health information listed was a contact at the Health and Disability Commissioner. The Committee advised that Māori health support is separate from the Health and Disability Commissioner and requested the inclusion of a dedicated Māori health contact. The Researcher apologised for the error and explained it was left-over from a previous template.
6. The Committee suggested the inclusion of a flow diagram or simple graphic to illustrate the study schedule as section detailing what participants are required to do is extensive.

Decision

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

* Please supply a new PIS for healthy volunteer participants.
* Please provide an updated main Participant Information Sheet, taking into account the suggestions made by the Committee.
* Please supply an updated protocol with sufficient detail to allow another research team to replicate the study. .

After receipt of the information requested by the Committee, a final decision on the application will be made by Professor Jean Hay-Smith and Ms Sandy Gill.

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| **12** | **Ethics ref:** | **19/STH/82** |
|  | Title: | M15-570: An Extension Study of ABBV-8E12 in Early Alzheimer's Disease |
|  | Principal Investigator: | Dr Nigel Gilchrist |
|  | Sponsor: | AbbVie Pty Ltd |
|  | Clock Start Date: | 25 April 2019 |

Dr Nigel Gilchrist and Larissa Roberts 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 a Phase 2 extension study, and is designed to evaluate the long-term safety and tolerability of ABBV-8E12 in participants with early Alzheimer's disease (AD). The study will consist of a 5-year treatment period and a follow-up period of approximately 20 weeks following the last study drug administration.
2. All participants who complete the Treatment Period in Study M15-566 will be eligible to participate in this study according to the selection criteria. Participants will receive study drug infusion every 4 weeks and undergo other study procedures and assessments, as outlined in the Study Activities Table in the protocol.
3. Participants who received placebo in Study M15-566 will receive 2000 mg ABBV-8E12 in Study M15-570.
4. Participants who received 300 mg ABBV-8E12 in Study M15-566 will receive 1000 mg ABBV-8E12 in Study M15-570
5. Participants who received 1000 mg or 2000 mg ABBV-8E12 in Study M15-566 will continue on the same dose in Study M15-570.

Summary of resolved ethical issues

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

1. The Committee queried how participants in the parent study were doing. The Researcher stated they were doing well with no ill effects. The Committee queried whether the schedule of events is similar between the two studies. The Researcher confirmed that it was and participants enrolling into the extension would know what to expect.
2. The Committee queried whether participants on placebo in the parent study would continue into the extension study blinded. The Researcher confirmed they would. The Committee queried whether these participants would receive the study drug. The Researcher confirmed all participants would receive the study drug (though doses may vary) and would remain blinded to this.
3. The Committee queried the response to question B.4.3. in the application which stated the Sponsor had placed restrictions on publication. The Researcher explained they could not publish without the Sponsor’s permission.
4. The Committee queried the response to question R.1.13.1 in the application and whether sites would be performing lumbar punctures. The Researcher stated lumbar punctures are being performed and if participants consent to them then they will be undertaken.
5. The Committee queried the response to question R.3.7 which discussed shipping blood samples to the Sponsor to be retained on site for 20 years. The Committee queried whether this was for the main mandatory samples or for the optional exploratory research samples. The Researcher clarified it was the optional research related to biomarkers which required participant consent. The Researcher confirmed the mandatory samples for the main study will be destroyed after 7 days, in accordance with the protocol and PIS.
6. The Committee noted the reproductive risks section was minimal. The Researcher stated it did not apply to any of the participants as they were all post-menopausal.
7. The Committee queried whether the Researcher knew any statistics regarding the prevalence of Alzheimer’s in Māori. The Researcher stated it was not nearly as prevalent in Māori compared to Pākehā but acknowledged this could be due to disparities in life expectancy. The Committee advised that for future applications this information would be useful to include in the response to question P.4.1.

Summary of outstanding ethical issues

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

1. The Committee noted the insurance policy encompassed the territory of Australia without explicit mention of New Zealand. The Committee queried whether the policy covered New Zealand. The Researcher stated they would confirm the insurance arrangements and provide an update to the Committee.
2. The Committee queried the scenario of a ‘study partner’ withdrawing their consent. The Researcher stated that without a study partner then unfortunately the participant would have to be withdrawn from the study. The Committee requested this be made very clear in the PIS that a partner withdrawing means the participant is withdrawn also.
3. The Committee requested the addition of a post-natal consent to the pregnant partner PIS as a parent cannot consent on behalf of their child until after the birth. The Researcher stated the sponsor had advised them that this was not necessary and did not need it for another study. The Committee advised that it is necessary and requested its inclusion. The Committee expressed concern at the sponsor’s attitude and requested the Researcher ensure the pregnant partner form from the parent study does include the post-natal consent. The Committee reiterated that under New Zealand law a baby is not a legal entity until after it is born. The Committee advised that it would need to review the form and could only grant provisional approval as a result of this.

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

1. The Committee advised that the Health and Disability Commissioner do not provide Māori health support and requested the contact details of dedicated Māori health support in the PIS. The Researcher agreed and stated they would use the CDHB’s Māori health support.
2. The Committee noted the cultural section in the PIS regarding tissue samples and discussion with whānau. The Committee advised this was the type of information it expects in response to question P.4.2 and suggested the Researcher include whakamā to their list.
3. Updates to the pregnancy PIS/CF, as noted in Point 15 above.

Decision

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

* Please update the Participant Information Sheet and Consent Form, taking into account suggestions made by the Committee.
* Please supply confirmation that the sponsor’s insurance is valid within New Zealand.

After receipt of the information requested by the Committee, a final decision on the application will be made by Dr Devonie Waaka and Mrs Helen Walker.

## 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:** | 11 June 2019, 11:45 AM |
| **Meeting venue:** | Sudima Hotel, Christchurch Airport, 550 Memorial Drive, Christchurch |

The following members tendered apologies for this meeting.

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

The meeting closed at 5 pm.