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| **Committee:** | Southern Health and Disability Ethics Committee |
| **Meeting date:** | 10 March 2020 |
| **Meeting venue:** | Sudima Hotel, Christchurch Airport, 550 Memorial Drive, Christchurch |

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| **Time** | **Item of business** |
| 11:15am | Welcome |
| 11:30am | Confirmation of minutes of meeting of 11 February 2020 |
| 11:45am | 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 – 4:45pm | 1. 20/STH/45 (Dominic / Devonie) 2. 20/STH/31 (Rochelle / Mira) [COI: Devonie] 3. 20/STH/40 (Dominic / Paul) [COI: Devonie] 4. 20/STH/33 (Pauline / Jean) 5. 20/STH/34 (Dominic / Mira) 6. 20/STH/35 (Pauline / Paul) 7. 20/STH/36 (Dominic / Devonie) 8. 20/STH/37 (Pauline / Jean) 9. 20/STH/38 (Rochelle / Devonie) 10. 20/STH/39 (Pauline / Jean) 11. 20/STH/43 (Dominic / Mira) 12. 20/STH/41 (Pauline / Paul) |
| 4:45pm | General business:  Noting section |
| 5:00pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Sarah Gunningham | Lay (other) | 05/07/2019 | 05/07/2022 | Apologies |
| Dr Devonie Waaka | Non-lay (intervention studies) | 18/07/2016 | 18/07/2019 | Present |
| Assc Prof Mira Harrison-Woolrych | Non-lay (intervention studies) | 28/06/2019 | 28/06/2020 | Present |
| Ms Rochelle Style | Lay (ethical/moral reasoning) |  |  | Present |
| 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 |
| Mr Dominic Fitchett | Lay (the law) | 05/07/2019 | 05/07/2022 | Present |
| Dr Pauline Boyles | Lay (consumer/community perspectives) | 05/07/2019 | 05/07/2022 | Present |

## Welcome

The Committee noted that apologies had been received from the Chair, Dr Sarah Gunningham. In accordance with the HDEC Standard Operating Procedure the Committee elected Dr Devonie Waaka as acting Chair for the duration of the meeting.

The Chair opened the meeting at 11:00 am and welcomed Committee members.

The Chair noted that it would be necessary to co-opt members of other HDECs in accordance with the Standard Operating Procedures. Ms Rochelle Style of the Northern A HDEC confirmed her eligibility, and was co-opted by the Chair as a member of the Committee for two applications.

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 February 2020 were confirmed as a true and accurate record of the meeting.

## New applications

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|  | **Ethics ref:** | **20/STH/45** |  |
|  | Title: | Phase 3 Study of Pembrolizumab and Lenvatinib in Combination with TACE for Incurable/Non-metastatic Hepatocellular Carcinoma (LEAP-012) |  |
|  | Principal Investigator: | Professor Ed Gane |  |
|  | Sponsor: | Merck Sharpe and Dohme |  |
|  | Clock Start Date: | 27 February 2020 |  |

Professor Ed Gane, Dr,Chirstine Crooks 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 randomised, double-blind, placebo-controlled study will evaluate the addition of lenvatinib and pembrolizumab to TACE as first-line treatment in advanced hepatocellular cancer.
2. The study aims to enrol 950 participants world-wide, with approximately 10 participants recruited 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 queried the response to R.2.1. in the application which stated that ‘deidentified and appropriate data would be shared with the sponsor before the study / pre-screening’. The Committee requested clarification as participant data cannot be shared with the sponsor before informed consent is provided. The Researcher stated this was an error and confirmed individual data would not be shared with the sponsor. The Researcher explained the answer was referring to general numbers only and not health information.
2. The Committee noted the response to R.3.1.2. in the application which stated that, should a participant withdraw from the study, all samples (including those for optional future research) would continue to be used unless specifically withdrawn. The Committee advised that the onus is on the study team to ask withdrawing participants what they wish to happen with their FUR sample and stated that consent to continued research cannot be assumed. The Researcher confirmed that withdrawing participants would be specifically asked if they wished for their samples to continue to be used.

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 requirement for mandatory biomarker and genetic analysis. The Researcher stated that study processes were designed for participants in an entire country to provide samples and in areas where ethics committees would not approve this as mandatory the country would not participate in the genetic analysis. The Committee queried why it was done by country and not by participant choice. The Researcher stated this had been discussed with the Sponsor headquarters who responded it was difficult to operationalise this down to the patient level and so it is a binary by-country opt in or out. The Committee stated that this raises a potential ethical issue: it will remove the choice from people in New Zealand who would otherwise say yes; and New Zealand participants / ethnicities would be excluded from any representation in the biomarker and genetic analysis. The Committee stated that optional donation of samples for genetic analysis should be offered to New Zealand participants. The Researcher agreed and stated they would consult with the Sponsor.
2. The Committee stated that it would be satisfied for the biomarker tests to be mandatory, provided these tests were limited to the scope stated in the submitted PISCF. The Committee noted that the PISCF stated biomarker analysis would be directly related to the current study aims or the disease under study.

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

1. The Committee requested the removal of the ‘yes / no’ boxes on the consent form for informing the participant’s GP of study enrolment and abnormal results of potential clinical significance. The Committee advised that in a study of this nature this should be mandatory.
2. The Committee requested a lay-friendly subtitle as the current one is too technical. The Committee noted the word ‘incurable’ is a confronting term. The Researcher suggested revising this to state ‘advanced’ liver cancer.
3. The Committee requested a revision to the reproductive risks to state participants can either be abstinent if in line with their preferred lifestyle or to use the recommended contraception. The Committee cautioned against including abstinence as a contraceptive method as it is unreliable.
4. The Committee noted the stool sample PIS discusses DNA testing. The Committee asked for it to be made clear whether host genetic testing was planned as part of the stool sample analysis, or if this referred to bacterial DNA analysis.
5. The Committee requested the inclusion of a statement advising participants that they would not benefit commercially from any subsequent discoveries or uses of the bacterial DNA.
6. The Committee noted the tumour tissue PIS discusses tissue samples and then biomarker and genetic samples. The Committee requested a revision to clarify this and suggested using the term ‘tissue sample’ throughout the document.

The Committee stated that if genetic analysis was planned for tumour tissue, this should be clearly explained in the Tumour Tissue PISCF.

1. The Committee advised that it does not have the capacity to review translated documents in languages other than English. The Committee advised it is up to the site to ensure these are accurate translations.
2. The Committee requested a revision of the PIS to check for spacing and formatting errors.

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 feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
* Please confirm that genetic analysis will be optional for New Zealand participants, and provide a suitable PISCF for optional donation of samples for genetic analysis.

After receipt of the information requested by the Committee, a final decision on the application will be made by Mr Dominic Fitchett and Dr Devonie Waaka.

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| **2** | **Ethics ref:** | **20/STH/31** |  |
|  | Title: | CH-ALV-2001: A study assessing variations in how quickly STELARA is processed and cleared by the body, in healthy adult males. |  |
|  | Principal Investigator: | Dr Chris Wynne |  |
|  | Sponsor: | Christchurch Clinical Studies Trust Ltd |  |
|  | Clock Start Date: | 27 February 2020 |  |

Dr Chris Wynne and Dr Richard Robson 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.

Dr Devonie Waaka declared a professional conflict of interest. The Committee agreed that Dr Waaka would step out of the room and would lose voting rights for the application.

Mr Dominic Fitchett was elected as Acting Chair for discussion of the application.

Summary of Study

1. This single arm pilot study will assess the inter-subject variability of single-dose subcutaneous Stelara (ustekinumab) administration in healthy male participants.
2. The results of the study will inform a proposed ustekinumab biosimilarity study.

Summary of resolved ethical issues

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

1. The Committee queried why more PK data was needed for an approved product with a previous study of 55 healthy volunteers. The Researcher stated they had performed an extensive literature search to obtain the PK data in order to calculate a sample size for a biosimilar study, but this information was not in the public domain. The Researcher stated they believe it would be unethical to perform a biosimilar study on healthy volunteers without knowing an appropriate sample size when the protocol was written, as the alternative would be to potentially expose more volunteers to the drug than necessary. The Researcher stated the Sponsor has requested the raw data from the previous study, but this has been declined.
2. The Committee noted the drug has been licensed in other markets so there must already be PK data. The Researcher stated the data held by regulatory authorities was confidential and there was not enough data in the public domain so on that basis it is scientifically reasonable to do the study.
3. The Committee stated it would have been helpful if the peer review had specified that there was not enough data in the public domain, as the review implied this was a biosimilar study. The Researcher clarified the reviewer was aware this was a study to obtain PK data from the originator medicine (Stelara) before a comparative biosimilar study.
4. The Committee queried when the original study was published. The Researcher stated it was in 2013, predating the requirement to make the raw data available and regulatory authorities such as the FDA will publish information on decisions but not the raw data. The Committee stated that from an ethical perspective it would support trying to obtain more information rather than initiating a biosimilar study with less. The Committee accepted on this basis the study is justified.
5. The Committee acknowledged the participant population was a small sample of healthy male volunteers but stated it still had concerns over the increased risk of infection and whether it was appropriate to expose participants to that level of risk. The Researcher stated they did not believe it to be a significant risk as they were healthy volunteers given a single dose. The Researcher stated in a STELARA randomised trial against placebo there was no statistically significant difference in infection rates. The Committee stated its concern was the increased risk of infection in participants in the context of a global pandemic. The Researcher stated they are mindful of COVID-19 and if it appeared the risk of infection to participants would increase, they would halt the study. The Researcher emphasised the informed process was long and involved discussion of all risks and as an investigator they have responsibilities not to harm participants. The Committee stated it was reassured that as a single dose study the risk of infection was lower than if it were multiple doses over time.
6. The Committee advised that with the roll out of the new National Ethical Standards for Health and Disability Research and Quality Improvement by NEAC there are increased requirements around data management and data governance. The Committee stated it did not have evidence of the study meeting these requirements. The Researcher stated they had been proactive and drawn up a data management plan as a parallel document that was not included in the protocol. The Researcher stated they had received legal advice to ensure it was compliant with Chapter 12 of the new standards. The Committee stated that they needed to see evidence of the data management plan in order to approve the study from an ethical perspective. The Researcher tabled the data governance plan for review. The Committee stated it was satisfied with the data governance plan.

Summary of outstanding ethical issues

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

1. The Committee considered vaccines which are and are not allowed and queried whether participation in this study would prevent participants from getting the flu vaccine. The Researcher stated participants could have the flu vaccine prior to enrolment, provided it was not administered within the protocol-specified exclusion window for all concomitant medications. Should a participant already on-study decide to have the seasonal influenza vaccine, they may be withdrawn from the study, as would be the case for a participant taking any concomitant medication during the study. The Committee requested a statement advising participants they can receive the flu vaccine prior to study enrolment. The Committee requested a reference to the flu vaccine as this is likely to be the only vaccine healthy men would typically be thinking of getting. The Researcher agreed to add this.
2. The Committee requested a revision to the reproductive risks to move abstinence in line with preferred lifestyle below the recommended contraception options. The Committee cautioned against including abstinence as a contraceptive method as adherence to it is unreliable.
3. The Committee requested the statement in the consent form that CCST has agreed to pay compensation be revised to state the participant understands the compensation provisions.

Decision

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

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

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| **3** | **Ethics ref:** | **20/STH/40** |  |
|  | Title: | GS-US-200-4330: A study comparing how fast the trial drug GS-6207 is processed and 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: | 27 February 2020 |  |

Dr Richard Robson and Dr Chris Wynne 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.

Dr Devonie Waaka declared a professional conflict of interest. The Committee agreed that Dr Waaka would step out of the room and would lose voting rights for the application.

Mr Dominic Fitchett was elected as Acting Chair for discussion of the application.

Summary of Study

1. This open-label study assesses the impact of severe renal impairment on the single-dose pharmacokinetics of GS-6207.
2. The study will enrol ten participants with severe renal failure, and ten participants with normal renal function matched for age, gender and body mass index.
3. Approximately 20 participants will be enrolled in the study world-wide, with New Zealand contributing approximately four participants.

Summary of resolved ethical issues

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

1. The Committee noted the application discussed reimbursement for the Christchurch nephrology department but not for the one in Auckland. The Researcher stated Auckland was a rescue site that may or may not be involved in the study. The Researcher confirmed if the Auckland site did become involved it would receive the same reimbursement.
2. The Committee noted there was no pregnant participant / partner PIS. The Committee queried whether the Researcher would develop one in the event a participant / partner became pregnant. The Researcher confirmed they would, although this was unlikely in this population.
3. The Committee advised that the onus is on the study team to ask withdrawing participants what they wish to happen with their FUR sample as consent to continue research on it cannot be assumed. The Researcher confirmed that, should a participant withdraw from the study, they would specifically be asked whether their samples could continue to be used.
4. The Committee queried whether Māori consultation had only been undertaken in Christchurch as Auckland was a backup rescue site. The Researcher confirmed this was the case and stated if the Auckland site were to be activated then the appropriate consultation would occur as part of the locality approval process.

Summary of outstanding ethical issues

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

1. The Committee requested the word ‘methylxanthine’ be substituted with ‘caffeine-like’ for simplicity.
2. The Committee recommended amending the reference to ‘168 hours’ on page 4 of the main PIS to simply state seven days or a week.
3. The Committee requested lay-friendly language when discussing reproductive potential. The Researcher agreed to adapt the [HDEC reproductive risks template.](https://ethics.health.govt.nz/system/files/documents/pages/template-for-reproductive-risks-in-participant-information-sheets-sep17.docx) The Committee recommended removing abstinence as a recommended method of contraception.
4. The Committee noted Essure was listed as a method of contraception. The Committee stated this was unlikely to be available in New Zealand and has been a controversial product. The Researcher queried if a potential participant had one would the Committee require them to have another method. The Committee stated its concern was the sheet may be interpreted to recommend the method but acknowledged that if individuals are happy with it that is their choice and would not want potential participants to think they must have it removed.
5. The Committee noted several typos in the PIS and requested a thorough proof-read to correct them. The Researcher confirmed this would be undertaken and would include correction of an error in the Schedule of Assessments table.
6. The Committee noted the FUR PIS referred to ‘your disease’ on the first page, which is not applicable to participants with normal renal function. The Committee requested a correction to address this.

Decision

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

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

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| 4 | **Ethics ref:** | **20/STH/33** |  |
|  | Title: | 0170 - Phase 3 Clinical Effect Durability of TD-9855 for Treating snOH in Subjects with Primary Autonomic Failure |  |
|  | Principal Investigator: | Prof. Timothy Anderson |  |
|  | Sponsor: | Theravance Biopharma Ireland Ltd |  |
|  | Clock Start Date: | 27 February 2020 |  |

Professor Timothy Anderson 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. This Phase 3, randomised withdrawal study will evaluate the sustained benefit in efficacy and safety of TD-9855 in participants with primary autonomic failure and symptomatic neurogenic orthostatic hypotension (snOH).
2. Approximately 258 participants will be recruited into the study worldwide. New Zealand will enrol an estimated seven participants.

Summary of resolved ethical issues

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

1. The Committee noted it is the study team’s responsibility to check if potential participants have heart problems that would exclude them.
2. The Committee requested a justification for a placebo group given the risks of placebo in this patient population. The Researcher stated that placebo was justified due to the lack of efficacious treatment for snOH. Prior to study enrolment all participants will be encouraged to use available non-pharmacological interventions, including adequate salt intake and compression stockings. The Researcher stated those randomised to placebo would still have a good chance of making it through the double-blinded placebo phase of the study.
3. The Committee requested confirmation that the initial approach regarding study participation would be made by a member of the potential participant’s clinical care team. The Researcher confirmed they would do this.
4. The Committee queried why health information would be stored for 25 years. The Researcher stated there was no specific intention to retain it for 25 years and that number was chosen to ensure it was stored for a long enough duration. The Researcher stated other countries require it to be 25 years so it is the default, but this can be changed in New Zealand if required. The Committee stated this was not necessary and it could remain at 25 years.
5. The Researcher confirmed the screening period was 28 days. The Researcher stated that stopping midodrine was not necessary until 7 days prior to Day 1, so a gradual dose reduction could be implemented for those participants taking midodrine prior to study entry.

Summary of outstanding ethical issues

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

1. The Committee queried why tissue samples would be retained for five years. The Researcher stated if a subsequent study did not match this one the samples may be re-analysed to confirm the validity of the original findings. The Committee requested a brief explanation of this in the PIS.
2. The Committee requested a revision to the caregivers’ PIS to refer to risks to the caregiver, rather than to the main participant.
3. The Committee noted the PIS states there will be 8 study visits, although there appear to be 9 on the schedule.
4. The Committee requested a revision of the phrase ‘if this study is right for you’ to be explicitly clear about what the inclusion requirements are.
5. The Committee requested the risk frequencies (if known) for adverse events be added, for both the study drug and rescue therapy (e.g. “Between 1 and 10 people out of 100 will experience the following..”).
6. The Committee noted it appeared that 66% of previous participants had experienced adverse events and requested a statement emphasising this in the risks section.
7. The Committee requested the inclusion of potential risks of the Tilt test and Valsalva test.
8. The Committee requested a clarification in the PIS as to whether any post-study access to the intervention (if beneficial) will be available to participants.
9. The Committee advised that in order to access health information of the baby of a pregnant participant / partner, additional consent must be obtained after the infant’s birth. The Committee advised that a baby is not a legal person with human rights until after birth and during the pregnancy the mother can only consent to her own health information. The Committee recommended the addition of an addendum to the pregnancy PIS, to consent to the baby’s information after the birth.
10. The Committee advised that terminating a therapeutic study for commercial reasons is not acceptable in New Zealand and requested any reference to this in the PIS be removed.
11. The Committee requested the removal of the ‘yes / no’ boxes on the consent form for informing the participant’s GP. The Committee advised that in a study of this nature this should be mandatory.
12. The Committee requested the addition of a lay-friendly study title to the PIS.

Decision

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

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

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| **5** | **Ethics ref:** | **20/STH/34** |  |
|  | Title: | A study of EDP-938 in Ambulatory Patients with Respiratory Syncytial Virus |  |
|  | Principal Investigator: | Dr Michael Williams |  |
|  | Sponsor: | PPD |  |
|  | Clock Start Date: | 27 February 2020 |  |

Dr Michael Williams 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 randomised, double-blind, placebo-controlled study will evaluate EDP-938 versus placebo, in ambulatory adults with Respiratory Syncytial Virus (RSV) infection.
2. 70 participants will be enrolled in the study worldwide, including approximately nine participants in New Zealand. Ethical approval has been obtained in four countries 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 queried the recruitment process. The Researcher stated participants would have to be referred by their GP. The Researcher stated the protocol specified that patients seen in general practice that fit the criteria and respiratory symptoms could be referred for consideration. The Researcher stated another potential method would be to reach out and contact participants from previous studies on record. The Committee suggested the Researcher may have to revise the recruitment method, as most people who go to their GP with a URTI will not get swabbed and in the current environment will want COVID-19 testing. The Researcher stated they were mindful of this and with different clinical and epidemiological criteria did not believe anyone who met the COVID-19 case criteria would be screened for the study. The Researcher stated they could communicate this to GPs.
2. The Committee queried whether personal protective equipment will be used. The Researcher stated it would and is part of the programme even when pre-screening. The Researcher stated they currently operate above the Ministry of Health guidelines.
3. The Committee queried whether the Researcher had experience with this type of study before. The Researcher confirmed they did and explained they have done studies on influenza vaccinations, treatment and surveillance before. The Committee stated it was reassured that the Researcher has experience and adequate infection control procedures.

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 response to question R.1.1. which stated the only side effect is a headache. The Researcher stated the Investigator’s Brochure only lists headaches. The Researcher agreed to revise the PIS to state headaches are known but other side effects are possible.
2. The Committee noted not all the contraceptive options in the PIS are available in New Zealand (e.g. spermicide). The Committee requested the Researcher adapt the [HDEC reproductive risks template.](https://ethics.health.govt.nz/system/files/documents/pages/template-for-reproductive-risks-in-participant-information-sheets-sep17.docx) The Committee recommended removing abstinence as a recommended method.
3. The Committee queried why samples would be stored for 25 years, as this seems unusually long. The Committee noted another part of the application stated samples would be destroyed upon completion of analysis. The Researcher stated their standard process was to destroy the sample after analysis and that data and clinical records are to be kept for 25 years, not the sample itself. The Researcher agreed to provide clarification.
4. The Committee requested the removal of the ‘yes / no’ boxes on the consent form for informing the participant’s GP. The Committee advised that in a study of this nature this should be mandatory.
5. The Committee noted the compensation provisions state that cover is limited only to the drug / placebo. The Committee advised that in order to meet ACC-equivalent cover the study will need to cover any injury related to any procedure or participation in the study. The Committee requested a revision to the PIS to address this.

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

1. p1. Please replace 'nasal discharge and congestion' with 'runny nose or blocked nose'; 'respiratory' with 'breathing' etc.
2. p2. Replace Qtip with cotton bud, as Qtip is not a widely used term in New Zealand.
3. p2. Please state what will happen if the participant is negative for RSV but positive for flu? Will appropriate care / medical advice be provided?
4. Please review the Consent Form clauses and simplify to include only those that apply to the pre-screening test.

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

1. p1. Please state in bold that this is the first time the study drug will be tested in people with RSV infection.
2. p2. Delete the final paragraph (references optional testing).
3. p3-6. Many terms used are not lay friendly and are, on the whole, unnecessary. Please replace:
   * 'respiratory rate' with 'breathing rate'
   * haematology and urinalysis with blood cells and urine tests
   * Q-tip (american) with cotton bud
   * electronic data capture handheld device with electronic diary
   * acetominophen (american) with paracetamol
   * RSV RNA quantitation with 'measure the amount of RSV present in your nose'
   * pharmacokinetic analysis with 'measure study drug levels'
   * RSV serology assessment with a lay term
   * 'metabolite and or further evaluation of the bioanalytical method' with 'study drug breakdown products and/or study drug laboratory test methods'
4. Please remove references to optional biomarker collection in this section.
5. p7. Most of the first paragraph is redundant (has already been stated earlier in the PIS). Please delete.
6. p8. Please re-write that reproductive risks section in more readily understandable lay language. It is suggested that the HDEC template is used for this purpose.
7. p10.Please delete the statement that cover is limited only to injury cause by the study drug / placebo.
8. p11. Please amend the statement regarding the participant's GP being informed to use NZ language (not 'personal physician') and to make it clear that informing the GP is a prerequisite of study entry.
9. p13. Please delete the reference to exploratory biomarker collection; and use lay terms as noted above to describe end-of-study assessments.
10. p13. Please delete reference to legal representatives.
11. Consent Form. Please amend such that the two optional clauses are marked as mandatory

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

1. Please state how long samples will be retained for.
2. Please state whether any genetic testing will be done on samples.
3. Please state whether samples will be collected at the same time as other study blood tests.
4. Please state whether participants can receive results of biomarker tests (the Committee assumes they cannot as the tests are exploratory).
5. Please state how samples will be identified.

The Committee requested the following changes to the Recruitment Material:

1. Please replace references to zip codes with post codes.
2. Please replace ‘physician’ (American) with ‘doctor’.
3. Please amend text about 'receiving at no cost', as this is not appropriate for a study where 50% of participants will be on placebo. Study participation and study-related care from a doctor should never be paid for. Instead state only that participants will be reimbursed for travel expenses.
4. Please delete text about health insurance; this is not relevant to NZ (Banner Ad).
5. The Committee requested any references to acetaminophen in any study documents, including the e-diary, be changed to paracetamol to be appropriate for a New Zealand context. If amending the e-diary is not possible, participants must be clearly informed that acetaminophen is paracetamol in New Zealand.

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 feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
* Please clarify the duration of sample retention. – [reference]
* Please update the advertisements, taking into account the feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.12).*
* Please ensure there is evidence of ACC-equivalent compensation available to all participants in the event of injury during the study. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 17.1).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Mr Dominic Fitchett and Associate Professor Mira Harrison-Woolrych.

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| **6** | **Ethics ref:** | **20/STH/35** |  |
|  | Title: | Emerging Biomarkers for Monitoring of Congenital Adrenal Hyperplasia |  |
|  | Principal Investigator: | Mrs Lauren Bresnahan |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 27 February 2020 |  |

Mrs Lauren Breshahan 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 aims to develop new tests for monitoring congenital adrenal hyperplasia.

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 justification for the secondary use of tissue for research purposes without consent. The Researcher stated because the lab performs routine testing there are a lot of samples in storage and patients have consented to monitoring. The Researcher stated it would be better to use existing samples rather than attempt to collect new ones.
2. The Committee acknowledged the study would examine new tests similar to the test a patient had already consented to, but it would also involve the collection of health information (and not just demographic data) along with the sample. The Committee stated this raises issues as the baseline is that consent ought to be obtained if it is able to be.
3. The Committee stated generally it could grant a waiver if the following conditions are met:

* It is not possible to get consent due to the age or quantity of the samples, seeking consent would impact on the scientific validity of the study (i.e. for epidemiological studies), or the act of seeking consent could cause undue anxiety or distress to those whose consent was being sought., and;
* No participant or their family would be disadvantaged by the inclusion of their sample, and;
* The public interest in the study outweighs the individual’s right to privacy.

1. The Committee queried how many samples the study would require. The Researcher stated they did not have a certain number but about 40 patients in New Zealand have received the diagnosis.
2. The Committee queried whether the Researcher could send an invitation letter out to participants to ask their consent to use their sample. The Researcher stated they could but this would involve accessing their personal information. The Committee noted that doing unconsented research would also involve accessing personal information.
3. The Committee advised that there is a high threshold to obtain a waiver of consent for secondary use of tissue. The Committee reasoned that this was not a large sample size; if the PIS was well written it would not confuse or distress people; and if some of the target population refuse it would not affect study results. The Committee advised that in order to conduct the study it would have to be redesigned to obtain consent for the use of tissue.
4. The Committee queried whether young Māori present with congenital adrenal hyperplasia. The Researcher confirmed they did. The Committee advised that Māori consultation would be required. The Committee recommended the Researcher get in contact with their DHB’s research office.
5. The Committee queried whether the peer reviewer’s comments had been addressed. The Researcher confirmed they had and stated the review sheet has a signature box for the reviewer to sign that they are satisfied with the response.
6. The Committee requested the Researcher explain both research objectives in the resubmission, particularly the second and how it will be fulfilled using the information collected.

Decision

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

* All health and disability research in New Zealand that may potentially involve Māori participants requires suitable consultation with Māori. Please supply evidence of Māori consultation to ensure the study is appropriate for a New Zealand context. This is especially important for studies that involve the use of human tissue. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 3.7).*
* Participation in research should be voluntary and informed consent should be sought. Please create a participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
* If there are scientific, practical or ethical reasons why consent cannot be obtained please include a strong justification for a waiver of consent *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.50).*

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| **7** | **Ethics ref:** | **20/STH/36** |  |
|  | Title: | M19-850 - Open-label extension of Upadacitinib to adults with moderate to severe Atopic Dermatitis |  |
|  | Principal Investigator: | Prof Marius Rademaker |  |
|  | Sponsor: | AbbVie Limited |  |
|  | Clock Start Date: | 27 February 2020 |  |

Professor Marius Rademaker 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 open-label extension study investigates the efficacy and safety of upadacitinib in adults with moderate to severe atopic dermatitis.

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 there was a maximum amount of reimbursement for travel. The Researcher stated people come from various distances, so it is typically in the range of $60 - $100 although they have paid for flights in the past.
2. The Committee noted a reference to skin biopsies and queried whether they would be part of the study. The Researcher explained they are in the protocol for the overall study but New Zealand would not participate in this aspect.

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 advised that the onus is on the study team to ask withdrawing participants what they wish to happen with their FUR sample as consent to continue research on it cannot be assumed.
2. The Committee noted the response to r.1.4 in the application form, which stated that an independent data safety monitoring committee (IDSM) would be utilised for the study. The Committee queried this, as the protocol makes reference to an independent cardiovascular adjudication committee only. The Researcher stated they believed there was a full IDSM so but would need to seek confirmation. The Committee requested that the IDSMC Charter be supplied.

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

1. The Committee advised that in a New Zealand context it is more appropriate to refer to trial “participants” rather than “subjects”. The Committee requested a revision of all references to subjects to be replaced with participants.
2. The Committee noted statements like “this is a phase 3b single arm open label extension” do not convey useful information to laypeople and requested a thorough revision to simplify the sheet into lay-friendly language.
3. The Committee noted the > and < symbols did not appear to print well and recommended the Researcher check the formatting if necessary.
4. The Committee queried a reference to rheumatoid arthritis on page 5/15 under ‘infections’. The Researcher stated this was an error leftover from a previous study and agreed to remove it.
5. The Committee noted a reference that inferred participants would need to pay for their medicines. The Committee queried whether this was applicable to New Zealand. The Researcher stated it was for the international context as standard care here was funded. The Committee requested this be removed from the PIS.
6. The Committee noted the reproductive risks section contained advice for women but little advising men of their responsibilities if they have a partner. The Committee requested additional information and a revision to explain the reproductive risks in lay-friendly terms. The Committee recommended adapting the [HDEC reproductive risks template.](https://ethics.health.govt.nz/system/files/documents/pages/template-for-reproductive-risks-in-participant-information-sheets-sep17.docx) The Committee also recommended removing abstinence as a recommended method of contraception.
7. The Committee requested the removal of the statement advising that compensation will not be available if the injury is caused by dupilumab, as this is not applicable to this study.
8. The Committee noted the data section was lengthy and complex, and requested insertion of the following simple statement at the end: “This means your coded data may be shared quite widely”.
9. The Committee requested the inclusion in the data section of a statement that “there is a risk that de-identified data could be re-identified. This is a small risk at the moment, but this could change at the future”
10. The Committee requested an option on the consent form for participants to receive a lay summary of the study results when available.

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

1. The Committee noted the optional FUR PIS paraphrased the same information several times and requested a revision to simplify it.

The Committee requested the following changes to the Pregnancy / Pregnant Partner Information Sheet and Consent Form:

1. The Committee advised that in order to access health information of the baby of a pregnant participant / partner there would need to be an additional consent after the birth. The Committee advised that a baby is not a legal person with human rights until after birth and during the pregnancy the mother can only consent to her own health information. The Committee recommended the addition of another signature box on the pregnancy PIS to consent to the baby’s information after the birth.

Decision

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

* Please update the participant information sheet and consent forms, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
* Please confirm whether an independent DSMC will be used for the study. If an IDSMC is planned, please supply the charter for this. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.25).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Mr Dominic Fitchett and Associate Professor Mira Harrison-Woolrych.

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| **8** | **Ethics ref:** | **20/STH/37** |  |
|  | Title: | The Metformin Aneurysm Trial |  |
|  | Principal Investigator: | Professor Greg Jones |  |
|  | Sponsor: | University of Otago |  |
|  | Clock Start Date: | 27 February 2020 |  |

Professor Greg Jones 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 randomised, double-blind trial assesses the use of metformin versus placebo in abdominal aortic aneurysm (AAA).
2. 2000 participants will be enrolled in the study, with approximately 650 participants recruited at New Zealand sites.

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 confirmation that the consent process would always be done face to face. The Researcher confirmed it would and explained the forms had been taken from the Australian study and apologised for any confusion.
2. The Committee queried why the study would not reimburse participants’ travel expenses. The Researcher stated it was due to lack of funds and offering reimbursement would be a barrier, though the study would try to accommodate as best it can. The Committee stated this was acceptable as long as it was explicitly clear in the PIS and participants understood they may be out of pocket due to travel and parking.
3. The Committee queried the inclusion / exclusion criteria and whether participants with a diameter greater or lesser than 39 mm were included. The Researcher stated participants with an aneurysm greater than or equal to 39 mm would be included.
4. The Committee queried how any discrepancies between study and clinical interpretation reports for a given ultrasound scan would be resolved. The Researcher explained the second reading would be done at the central site and any discrepancies would be reported back to the site’s clinical lead for review.
5. The Committee queried the scenario of a blood test during screening returning a result of clinical significance. The Researcher stated this would be treated as per normal clinical management.
6. The Committee advised the CRF documents had been received but are outside of HDECs scope of review so have not been assessed.

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 tissue would be disposed of or stored for ten years as the application gave conflicting answers. The Researcher stated the samples would only be used for analysis related to this study**.**
2. The Committee advised the optional biomarker sample collection should be provided as an addendum to the main consent form, or a separate document. This must include: what biomarkers are; whether genetic testing is intended (and how extensive that may be); where samples will be stored and analysed; how they (and resulting data) will be identified; and how long they will be retained for. Please ensure a Māori tissue statement is included.
3. The Committee noted the supplied peer review was an NHRC letter which included some scientific review but did not give much context. The Committee stated it would usually expect to see the reviewer’s comments if it was an HRC review. The Researcher stated HRC assessment had been undertaken and agreed to supply the reviewers’ comments.

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

1. The Committee complimented the Researcher on the PIS as it is well written for lay readership.
2. The Committee requested an option on the consent form for participants to receive a lay summary of the study results when available.
3. The Committee requested information on data use and confidentiality be added to the PIS (e.g. will the data be coded and how, who will have access and why, how long it will be stored etc).
4. The Committee requested a statement advising participants that after 6 weeks their suitability would be assessed and they may not be able to continue in the study. The Committee requested removal of the statement about if participants ‘are happy’ to continue as this may not be their decision.
5. The Committee noted that if participants withdraw the study may continue to use data collected on them up until that point. However, the onus is on the study team to ask withdrawing participants what they wish to happen with their tissue sample, as consent to continue research on it cannot be assumed. The Committee requested information explaining this be added to the PIS.
6. The Committee requested a revision of the PIS to tidy up formatting.
7. The Committee requested a statement reminding participants that they may withdraw at any time and do not have to remain in the study when discussing long term commitments.
8. The Committee requested a revision of the side effects on the PIS. Page 4 refers to mild side effects whereas page 5 refers to the emergency department and there is crossover (e.g. nausea, diarrhoea, vomiting, stomach pain). The Committee requested this be amended into mild and severe side effects along with the frequencies (e.g. between 1 and 10 people in 100).
9. The Committee requested the removal of the ‘yes / no’ boxes on the consent form for informing the participant’s GP. The Committee advised that in a study of this nature this should be mandatory.

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 feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
* Please supply an independent peer review for the current version of the study protocol. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.26).*

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

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| 9 | **Ethics ref:** | **20/STH/38** |  |
|  | Title: | A Study of Nivolumab or Placebo in Combination with Docetaxel in Men with MetastaticCastration-resistant Prostate Cancer |  |
|  | Principal Investigator: | Dr Navin Wewala |  |
|  | Sponsor: | Bristol-Myers Squibb |  |
|  | Clock Start Date: | 27 February 2020 |  |

Dr Navin Wewala 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. This is a Phase 3, randomised, double-blind study of docetaxol and prednisone plus either nivolumab or placebo in metastatic castration-resistant cancer.

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 advised that the Sponsor’s wish to follow participants up, while understandable for scientific reasons, needs to be balanced against the participants’ right to withdraw, especially as it involves a third party company in the United States tracking people down. The Committee advised that this should not be a mandatory aspect of the study and should instead be an option on the consent form for participants to opt-in to.
2. The Committee requested an “If I am lost to follow-up I am happy to be traced and contacted by an American third party” option on the consent form.
3. The Committee noted the researchers must comply with the Chapter 12 of the new Standards, especially around data governance and management and issues which are required to be addressed in the information sheets and consent forms. All documentation should be reviewed with Chapter 12 in mind. Examples include but are not limited to:

* The data FUR PIS must comply with the new Standards, especially, but not limited to, Standard 7.57
* The PIS states “How Your Data Will Appear. Your name and contact details will be replaced by your initials along with your study number.” Participant initials must not appear on study documentation – only the unique identifier.
* The Sponsor must not have direct access to participant records as currently stipulated in Appendix 2 to the protocol Page 106: “The consent form must also include a statement that BMS and regulatory authorities have direct access to participant records”. If this refers to review of records for audit purposes, this must be clearly stated.
* The breadth of people accessing identifiable data is wide and, in some case, requires justification – refer, for example, to the answers given on the submitted form (r.2.2) – medical records staff, hospital staff involved with the participants (these people are listed separately to the research staff and investigators)
* Participant names must not be included on the questionnaires – only study ID (eg, BIp (short form includes name and initials; whereas the FACT-P (v4) and EQ-5D-5L have nothing, not even a study number))
* In what circumstances could it be impossible for a unique code to be assigned to participant information before it is provided to the research sponsor, its agents, third party contractors and business partners? Please provide justification for this or remove.
* What is going to India and why? Reference is made to India in the main PIS.
* Discuss the prevention of participant access to data until the study has concluded as stated in the main PIS – access should be allowed at any time, but it should be made clear to the participant that it will break the blind and they will have to leave the study.
* the patient alert card – includes the participant’s name and study id – note that a sponsor telephone number is given on the card – this means that, potentially, the sponsor may identify the participant. Is it usual to include the participant’s name on these cards?
* Reimbursement either from the site or through Greenphire. If it is to be Greenphire, participants need to know how much information they will have to give to Greenphire – eg, name, address and DoB and the name of the trial. Do participants become registered on Greenphire’s website? Are their names deleted once the study is over – ie, so there can be no further use of their contact details?

1. Tissue management and biobanking: The researchers must comply with the Chapter 14 of the new Standards which relate to human tissue and Chapter 15 which relates to biobanking. All documentation should be reviewed with Chapters 14 and 15 in mind and all PISCFs should be amended accordingly. Examples include but are not limited to:

* The Tissue Future Resarch (eg, biome) PIS must comply with the new Standards, especially, but not limited to, Standard 7.58
* the name and address of the central laboratory in Singapore and ICON must be given.
* there are three circumstances outlined in the PIS regarding what happens to tissue upon participant withdrawal, none of which appear appropriate: (a) “The Sponsor has already given the samples and information to external researchers for use in additional research”; (b) “When the study doctor no longer has the re-identifiable master list; and (c ) or “When the Sponsor has deleted the patient’s coded identification information in an effort to further protect their identity”. Please justify each of these situations.
* The description of the uses to which the tissue may be put in the main PIS are unacceptably wide and must be narrowed so that future unspecified research is optional. For example, it is too wide to state that that if a participant withdraws consent the samples will still be used for “ for other future or current research involving the same drug/s, the same or related therapeutic area, or for other relevant health research that is within the scope of the current research protocol.” Only the last descriptor is appropriate for inclusion in the main PIS.
* Statements made with in the PISs must be consistent – examples include, but are not limited to, the statement that third party biobanks such as ICON will only use the samples for the purposes of the study compared to the statement which seeks to expand out the scope of the main study to future unspecified research. Appropriate warnings must be included for participants so they are aware that there may not be NZ representation on the biobanks in Singapore which means that overseas researchers may not work with data in a way that is culturally appropriate for the New Zealand context, or have connections or understanding of the communities that the data relates to. (Standard 12.16 and 12.17)
* Plans must also be in place for incidental findings in the context of human tissue, consistent with Standards 14.23 – 14.26

1. The Committee noted the PIS inferred that if an injury was caused by the study drug there would be no insurance cover which is unacceptable in New Zealand. The Committee advised that all commercial trials in New Zealand must have ACC-equivalent insurance in place for all participants.
2. The Committee stated it was disappointed with the application’s consideration of Māori, with no acknowledgement that Māori have significantly higher mortality than non-Māori men with prostate cancer. The Committee requested the Researcher include relevant demographic statistics with any future applications.
3. The Committee stated it is generally expected for Researchers to collect ethnicity data when undertaking research in New Zealand.
4. The Committee queried the follow-up by phone process and what this would involve. The Committee requested additional information explaining this be added to the PIS.
5. The Committee noted no evidence of CI indemnity was included in the application. The Committee requested this be supplied with resubmission in order to ensure protection for the Researcher.
6. The Committee noted no independent peer review was supplied with the application. The Committee requested an approval letter from SCOTT be supplied with the resubmission.

Decision

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

* Please update the participant information sheet and consent forms, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
* Please supply an independent peer review for the current version of the study protocol. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.26).*
* Please supply evidence of ACC-equivalent compensation available to all participants in the event of injury during the study. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 17.1).*
* Please supply a data governance plan to ensure the safety and integrity of participant data

*National Ethical Standards for Health and Disability Research and Quality Improvement, paras 12.14 and 12.15).*

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| **10** | **Ethics ref:** | **20/STH/39** |  |
|  | Title: | Evaluation of the Nu Vera ICE Catheter during Percutaneous Procedures via transseptal puncture |  |
|  | Principal Investigator: | Dr Ian Crozier |  |
|  | Sponsor: | NuVera Medical |  |
|  | Clock Start Date: | 27 February 2020 |  |

Dr Ian Crozier 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.

Dr Paul Chin declared a potential conflict of interest which was deemed minor and the Committee decided to allow him to participate in the discussion and retain voting rights.

Summary of Study

1. This First in Human, single arm study evaluates the NuVera Intracardiac Echo Probe in percutaneous left atrial procedures with transseptal puncture.
2. The study will enrol 25 participants internationally, with approximately 10 participants anticipated 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 noted the response to B.1.2. in the application which states that ‘Not all hospitals use ICE routinely but effectively use X-rays alone’. The Committee queried if X-rays are effectively used alone why the catheter is necessary. The Researcher stated one reason it is not used routinely in New Zealand is due to the additional cost. The Researcher stated the catheter is commonly used in the United States during a transseptal puncture because the additional information improves safety of the procedure.
2. The Committee queried why the study was necessary if the procedure is routinely used elsewhere. The Researcher stated they wanted to prove that this catheter provides superior imagery to currently available probes and to X-rays alone and is therefore a better option.
3. The Committee queried the process for incidental findings. The Researcher stated they would be managed as per standard clinical practice.
4. The Committee queried how potential participants would be informed about the study and who would conduct the informed consent process. The Researcher stated the research team would identify potential participants, but their clinician would introduce the study and undertake the informed consent process.

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 protocol described this as a first in human study, and states that bench testing and pre-clinical studies were underway with some results still pending. The Committee noted the investigator brochure stated that clinical use would only begin when all design testing was complete. The Committee queried whether this had been completed. The Researcher stated they believed so but would need the Sponsor to confirm.
2. The Committee noted this was a multicentre study to be conducted in three countries. The Committee stated it would usually expect to see a sentinel enrolment whereby the device is used in one participant first, followed by a window to ensure the procedure is safe before being used in another participant. The Researchers agreed this was reasonable. The Committee requested an update to the protocol to include a sentinel enrolment schedule.
3. The Committee queried the process for reporting safety signals of concern. The Researcher stated the study team would notify the Sponsor of any significant issues who would then notify all sites within 24 hours. The Researcher stated it was implicit in the protocol but could be specified. The Committee requested the safety reporting process be formally protocolised.
4. The Committee noted the application stated an internal medical advisory committee may be created. The Researcher stated it was a small company and small study so was done on a smaller scale. The Committee stated it was acceptable to be internal, but it would expect all lead investigators to be part of it. The Researcher stated this was the plan and could be added to the protocol. The Committee requested it be formally protocolised.
5. The Committee queried the scenario of the catheter not providing adequate views. The Researcher stated that if the ICE catheter did not give a satisfactory view, they would withdraw the catheter and go back to the conventional method used as standard of care. The Committee requested information explaining this be added to the PIS.

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

1. The Committee requested the addition of a lay-friendly study title to the PIS.
2. The Committee noted it could be difficult to understand what happens during the study from a lay perspective. The Committee recommended the inclusion of a diagram to assist.
3. The Committee requested a revision to the risks section to make it more lay-friendly to ease participant understanding.
4. The Committee stated informing each participant’s GP should be a mandatory aspect due to the nature of the study. The Committee requested the removal of the ‘yes/no’ boxes for the option of informing the participant’s GP.
5. The Committee requested the addition of a separate statement on the front page of the PIS advising potential participants that this will be the first time the device is tested in humans.
6. The Committee advised that HDEC is not a regulatory authority and requested removal of the statement about the study being approved by regulatory authorities.
7. The Committee requested the addition of information explaining the alternatives to participation in the study (e.g. normal standard care in Christchurch / X-ray guidance).
8. The Committee requested the addition of information explaining who participant data would be shared with and how long it would be stored.
9. The Committee queried a statement in the PIS mentioning a Sponsor representative being present for data collection. The Researcher explained the representative would provide technical support and ensure the data is collected to the Sponsor’s requirements. The Committee requested an explanation of this is added to the PIS.
10. The Committee requested the inclusion of a Māori health contact number in the PIS.
11. The Committee requested a lay-friendly explanation of the difference between ‘3D and 4D images’ and a thorough revision to rewrite medical / technical terminology.
12. The Committee requested a revision to correct any formatting issues.

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 feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
* Please update the study protocol, taking into account the feedback provided by the Committee. Specifically, please introduce a sentinel dosing schedule to ensure participant safety and a section detailing safety reporting. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).*

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

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| **11** | **Ethics ref:** | **20/STH/43** |  |
|  | Title: | “Transcranial electrical stimulation for early Alzheimer's disease.” |  |
|  | Principal Investigator: | Dr Divya Adhia |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 27 February 2020 |  |

Dr Divya Adhia 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 feasibility study assesses the use of brain stimulation therapy in participants with early Alzheimer’s disease.
2. 20 participants (and their carers) will be recruited into the trial, which will be conducted at a single New Zealand site.

Summary of resolved ethical issues

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

1. The Committee noted the peer reviewer had concluded the sample size was not large enough to determine efficacy and advised keeping the study simple to evaluate feasibility and anything additional can be done in a future study. The Researcher agreed this was a sensible approach.
2. The Committee queried the reason for maintaining electronic data without the participant’s name for 10 years and what this was intended for. The Researcher explained it is University policy that data needs to be stored for 10 years without an identifier. The Researcher stated there would be a unique study ID code attached to it.
3. The Committee queried whether the audio recordings would be kept. The Researcher confirmed they would be destroyed upon transcription.
4. The Committee suggested the Researcher consider giving the petrol vouchers halfway through the study to assist with expenses rather than at the end as some participants may be on a limited income.

Summary of outstanding ethical issues

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

1. The Committee queried the risk of seizure. The Researcher stated it would be minimal risk as this is a safe technique. The Researcher explained another study approved by HDEC on 25 volunteers did not produce any adverse events. The Committee requested this be added to the PIS to provide potential participants with more information.
2. The Committee noted the response to F.2.3.1 in the application which indicated that participants in the sham group would be offered the opportunity to undergo the active stimulation protocol if they wished to. The Committee queried whether this was part of the research study or something separate. The Researcher stated it was not part of the study, but they wished to extend the opportunity to those who did not receive the stimulation to do so. The Committee stated the concern was as the study is trying to establish the utility and safety of the stimulation that offering it before the results are analysed may be premature. The Researcher stated they wished to make it available so everyone would have access but can change this. The Committee recommended a revision to state that if this or subsequent studies show stimulation is beneficial then it may be offered, but not to guarantee an automatic offer.
3. The Committee requested a lay-friendly title which avoids the use of technical language such as ‘cognition’.
4. The Committee requested a revision of the PIS to simplify the language e.g. on page 2 when providing contact details to the GP revise it to ‘we will tell your GP you have agreed to be in this study’.
5. The Committee requested references to ‘adverse effects’ be amended to ‘side effects’ as a more lay-friendly term.
6. The Committee requested the references to receiving care and informing the participant’s GP be removed from the caregiver PIS as these are not applicable.

Decision

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

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

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| **12** | **Ethics ref:** | **20/STH/41** |  |
|  | Title: | Scabies survey and case-control study |  |
|  | Principal Investigator: | Dr Simon Thornley |  |
|  | Sponsor: | Health Research Council New Zealand |  |
|  | Clock Start Date: | 27 February 2020 |  |

Dr Simon Thornley 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 has several aims: to undertake a survey of scabies prevalence in Auckland children attending educational institutions; to undertake a case control study of scabies and acute rheumatic fever; to compare methods of diagnosing scabies infection; and to acquire images of scabies-affected skin for a mobile app library.
2. The survey will recruit 2100 children and adolescents, with an additional 100 cases (participants with acute rheumatic fever) enrolled in the case-control substudy.

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 GPs would be involved. The Researcher stated they would be informed but the study would have its own GP treating participants. The Committee noted references to ‘family doctor’ and ‘research doctor’ in the PIS and requested these be clarified.
2. The Committee queried how suspected scabies in a participant would be managed. The Researcher stated there was little gap between the questionnaire and examination and so the GP would write a prescription and the study staff would contact the family to arrange treatment.
3. The Committee queried whether the questionnaire would apply to family members. The Researcher stated yes as the intention was for the parents to fill it out. The Committee queried about any other relatives or people living in the house and if they would fill it out. The Researcher stated no and explained the intention was for one person to fill it out on behalf of the family.
4. The Committee queried the scenario of a parent having scabies. The Researcher stated if the responses indicated other family members did have scabies, they could arrange treatment, although the focus is on the child. The Committee queried whether it would be possible to make a diagnosis via the questionnaire as it could be non-specific and families would likely answer yes to bites, scratches, itch etc. The Researcher stated it is not a scenario they had considered as the research is primarily about the child rather than the family, although if a child did have scabies, they would recommend treatment for the family. The Committee queried whether the study had enough resources to follow up family members. The Researcher stated likely not, and they would need to refer family members to their GP for follow-up.
5. The Committee queried whether the study would limit recruitment to Māori and Pasifika children. The Researcher stated no, all children attending educational institutions in Auckland would be eligible. The Committee stated the PIS is written in a way which implies that it is limited to Māori and Pasifika people. The Committee requested a revision to rename the study and remove the emphasis on Māori and Pasifika.
6. The Committee requested a safety protocol for researchers attending home visits. The Researcher agreed to develop one.
7. The Committee queried how an unexpected positive result from the test in Australia would be managed. The Researcher stated they would follow up on it and the information is in the protocol. The Committee requested this information be included in the PIS so participants are aware.
8. The Committee queried how the study would engage with schools to participate. The Researcher stated they would work with each selected educational institution. The Researcher stated they have a list of schools and will randomly select and invite schools to participate. If the school accepts the invitation, they will select classes within the schools and invite students to participate.
9. The Committee queried the age range of students eligible. The Researcher confirmed it the study could include new entrants through to the end of high school. The Committee advised that if any students turn 16, they will be able to consent for themselves and will need their own unique PIS separate to the parents one.
10. The Committee advised that if family members will be asked to provide samples or information this would make them participants and requested another PIS for them to read and sign before any screening.
11. The Committee queried whether the study team would inform the school of a positive scabies diagnosis. The Researcher stated they would not, although they would inform the parents of their responsibilities in terms of treatment. The Committee requested the insertion of a statement into the PIS stating the school will not be informed as some parents may not wish the school to know.
12. The Committee queried whether prescribed treatment participants would receive is fully funded. The Researcher confirmed it is. The Committee requested this be added to the PIS so participants are aware it is funded.

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

1. The Committee requested information explaining that the skin samples sent to Australia for testing will be destroyed after testing.
2. The Committee requested information advising participants that their data may be used to develop the mobile app and they will not receive any commercial rights or benefits if their information is used this way.
3. The Committee requested the removal of the ‘yes / no’ boxes on the consent form for informing the participant’s GP. The Committee advised that in a study of this nature this should be mandatory.
4. The Committee requested an option on the consent form for participants to receive a lay summary of the study results when available.
5. The Committee stated the rheumatic fever PIS was confusing and requested any references to it being a ‘substudy’ be removed as for participants with rheumatic fever this would be the only study. The Committee advised that family members would also need their own PIS, and children would need their own assent form for this.
6. The Committee requested the Researcher include information on what cleaning needs to be done in the event of a positive scabies result (e.g. wash all clothing, bedding or vacuum furniture etc).
7. The Committee noted the invitation stated informed consent would be obtained in the participant’s house and queried whether this was for everyone. The Researchers stated this was only for the case control. The Committee requested a revision to clarify.
8. The Committee requested a revision of the statement that children can say no and they won’t get in trouble, to clarify that if the child does not want to participate they do not have to. The Committee requested a statement in the parent PIS informing them that even if they wish their child to participate, if the child says no they do not have to.

Decision

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

* Please update the participant information sheet and consent forms, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*

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

## 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:** | 14 April 2020, 11:45 AM |
| **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. **Matters Arising**
2. **Other business**
3. **Other business for information**
4. **Any other business**

The meeting closed at 5:00pm.