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| **Committee:** | Southern Health and Disability Ethics Committee |
| **Meeting date:** | 11 August 2020 |
| **Meeting venue:** | Via videoconference |

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| **Time** | **Item of business** |
| 11:30am | Welcome |
| 11:35am | Confirmation of minutes of meeting of 14 July |
| 11:40am | New applications (see over for details) |
| 11:45 – 12:10pm  12:10 – 12:35 12:35 -1:00  [15 minute Break]  1:15 – 1:40  1:40 – 2:05  2:05 – 2:30  2:30 - 3:00 | i 20/STH/122 ii 20/STH/121  iii 20/STH/123  iv 20/STH/126  v 20/STH/124  vi 20/STH/125  vii 20/STH/119 |
| 3:00pm | General business:  Noting section |
| 3:10pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Sarah Gunningham | Lay (other) | 27/10/2015 | 27/10/2018 | Present |
| 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 | 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 (other) | Acting | Acting | 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 | Apologies |

## Welcome

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

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 14 July were confirmed.

## New applications

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| **3** | **Ethics ref:** | **20/STH/122** |
|  | Title: | Evaluation of Efficacy and Safety of PLN-74809 in patients with Idiopathic Pulmonary Fibrosis |
|  | Principal Investigator: | Professor Lutz Beckert |
|  | Sponsor: | Worldwide Clinical Trials on behalf of Pliant Ther |
|  | Clock Start Date: | 30 July 2020 |

Prof Lutz Beckert was present via videoconference for discussion of this application.

Potential conflicts of interest

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

Dr Paul Chin and Dr Devonie Waaka both declared conflicts of interest, and the Committee determined that they were not substantial and that both would remain and participate in the discussion.

Summary of Study

1. This is a Phase 2a, multicentre, 3-part, randomised, double-blind, dose-ranging, placebo-controlled study evaluating the safety, tolerability and pharmacokinetics of daily administration of PLN-74809 for up to 12 weeks in participants with idiopathic pulmonary fibrosis (IPF).
2. Each part consists of a screening period, a 4 week (Part A) or 12 week (Parts B and C) treatment period, and a 1-week post treatment follow-up period. Part A has completed recruiting and therefore New Zealand will be participating in Part B.
3. In part B, approximately 28 eligible participants will be randomised in a 3:1 ratio (active:placebo) to receive either 40mg of PLN-74809 or matching placebo administered orally once a day.
4. Part C plans to evaluate up to 2 additional PLN-74809 dose cohorts (higher than 40mg but not exceeding the daily concentration limit of unbound PLN-74809) based on the following criteria:

1) Part B has fully enrolled

2) favourable review by the DSMB of a) all available safety and PK data from parts A and B of this study, plus all safety and PK data from an ongoing phase 1 study in healthy participants (PLN-74809-104).

1. The main purpose of this proposed study is to confirm that PLN-74809 is well tolerated by participants with IPF, whether as monotherapy or as an add-on to standard of care (SoC) with pirfenidone or nintendanib, and that the drug concentrations are similar to those previously found in healthy participants. The study will also test, in an exploratory manner, a panel of biomarkers with potential to assess drug effect as well as attempt to identify trends in typical IPF efficacy and patient-reported outcomes.

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 how participants would be randomized to either standard of care, monotherapy or placebo. The Researcher explained that patients originally may be on no active treatment, pirfenidone or nintendanib, and in any case could be randomized to the study drug or placebo.
2. The Committee asked what would happen to participants’ samples if they withdraw their consent. The Researcher said that tissue used for the main study would be destroyed after use, and that samples donated for future unspecified research would be anonymized and therefore could not be withdrawn.
3. The Committee asked about the potential benefit that the study could bring for Māori. The Researcher stated that there is only limited data about the prevalence of IPF in Māori, and that this study, due to involving such a small number of participants, is unlikely to benefit Māori.
4. The Committee noted that a number of the answers to questions in the application form were not accurate or were answered incompletely, and as such the application form could not be regarded as a study document.
5. The Committee asked how patients would be informed about and invited onto the study. The Researcher explained that he would inform his medical colleagues about the study, who would then inform any patients about the study who would be eligible. If they express an interest in participating, the CI would then contact them and provide greater information about the study.
6. The Committee asked for an MPS certificate, or equivalent, to be provided for the Coordinating Investigator.
7. The Committee noted that the Sponsor insurance certificate was not New Zealand-specific, however given the low number of participants in the study the Committee agreed that it was satisfied that the insurance was sufficient.
8. Committee stated that the study cannot stop for commercial reasons.

Summary of outstanding ethical issues

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

1. The Committee asked for clarification regarding the different phases of the study mentioned in the study documentation, and in particular whether the participants with which this ethics application is concerned would be enrolled in part B only, or potentially also in Part C.
2. The Committee requested greater information about how data will be managed.

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

1. All forms:
   * Please use a simple title appropriate for a lay audience.
   * Please review the formatting, and amend for legibility.
2. PISCF (Main)
   * Please review the document and remove all repeated sections, e.g. the information about dosing, fasting and blood volumes.
   * Page 9: where it mentions allergic reactions which indicate anaphylaxis, please state that participants should contact the emergency services (not their study doctor).
   * Please improve the reproductive risks section, and refer to the HDEC reproductive risks template for guidance.
   * Please remove the text which has been added to the HDEC template wording in the compensation section, as some statements are at odds with the Research Medicines Industry guidelines and responses provided in the application form.
   * Page 12: the statement is "Expenses (e.g. travel) may be reimbursed, after receipts for the payments are provided, and in agreement with the study doctor." Study expenses should be reimbursed, please amend to "Expenses (e.g., travel) will be reimbursed, after receipts for the payments are provided, and in agreement with the study doctor" (or similar).
   * Please simplify the data section and especially the parts about confidentiality and privacy to make them easier to understand, and refer to the new HDEC PISCF template for guidance.
   * Please make clear what data is being provided to authorized personnel, and who they are. In each case where data is being accessed it should be specified in what form (identifiable, de-identified, etc)..
   * Page 15: please note that health information is required to be kept for at least 10 years in NZ.
   * Please state that participants can request the withdrawal and destruction of samples.
   * Page 18 consent form: please remove Yes/No options as these are not really optional (according to the PIS).
   * Page 18 consent form: please remove the option and make it mandatory for the GP to be informed of a participants’ participation.
   * Please remove the information about future unspecified research from the PIS on pages 5 and 11, as well as the optional tick box in the consent form.
3. Optional Pharmacogenomics PIS:
   * Please remove the statement that DOB will be collected.
   * “What happens to my samples”: please proof-read and simplify this section.
   * Please clarify whether broad testing, such as whole genome analysis, may be performed.
   * Please state whether the testing will be clinically relevant/actionable.
   * Study withdrawal section: please remove any information that is not relevant to donating a blood sample for pharmacogenomics research.
   * Data section: please review for clarity of information and refer to the HDEC PISCF template for guidance.
   * Page 4: please note the sponsor may not stop a therapeutic study for commercial reasons in NZ.
   * Page 6: please include a Yes/No option for "I want my identity to be removed from my (blood and urine) samples and understand that in this case I will not be able to withdraw my consent in the future".
   * Page 7: please remove the current Yes/No option as this is not really optional (according to the PIS).
4. Future Unspecified Research PISCF:
   * Many of the issues noted with the pharmacogenomics PISCF also apply to the FUR PISCF. Please review and amend as indicated..
5. Pregnant partner PIS:
   * Please ensure that the data section complies with standard 12.15.a of the National Ethics Standards, and refer to the HDEC PISCF for guidance.
   * Please state that participating will not impact the male participants’ standard medical care or their continuation in the study.
   * Please state whether the pregnant partner is able to find out if the male participant received (or is receiving) the active drug or placebo.

Decision

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

* Please upload a cover letter clarifying the different phases of the study and which parts are relevant for this application.
* Please submit a data management plan, in accordance with standard 12.15a of the National Ethical Standards.
* Please amend the Participant Information Sheet and Consent Forms, taking into account the recommendations made 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 Sarah Gunningham and Dr Devonie Waaka.

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| **2** | **Ethics ref:** | **20/STH/121** |
|  | Title: | Gluco-Light: Pulse-glucometery clinical proof of concept study |
|  | Principal Investigator: | Dr Jennifer Knopp |
|  | Sponsor: | University of Canterbury |
|  | Clock Start Date: | 30 July 2020 |

Dr Jennifer Knopp was present via videoconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

* This study aims to assess the accuracy and usefulness of a novel light-based and non-invasive glucose monitor in a neonatal cohort. The sensor works on the same principles as a pulse-oximeter, but uses several other wavelengths of light to calculate the concentration of glucose in pulsatile blood-flow (pulse-glucometry).
* This study will use a blinded light-based glucose sensor to record pulse-glucometry waveforms (intermittently) alongside normal-care glucose measurements. The waveforms will be retrospectively analyzed and calibrated to generate a glucose measurement value, which will then be compared to the paired clinical glucose measurement. Such outcomes will provide proof-of concept outcomes for the use of this sensor in a neonatal cohort.

Summary of resolved ethical issues

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

* The Committee congratulated the researcher on producing a well-put together application.
* The Committee stated that the answer given to question R.1.1 was not correct, and asked for clarification as to whether the study is being conducted for commercial benefit. It was agreed that the study is a proof of concept study, and is being conducted primarily for the purpose of a PhD. Although commercial benefit is anticipated if the trial shows positive results, that would mostly be incidental to the current study. As such, participants are expected be covered by ACC.
* The committee asked if there was the possibility of incidental clinically relevant findings, due to the device not working well on certain patients. The Researcher stated that if such a finding was made, it would not be immediately obvious and would likely not be actionable by the research team.
* The Committee questioned the answer to question P.2.1, which stated that the researchers would be approaching people in antenatal clinics. The Researcher stated that this was incorrect and people would be approached after the birth of the baby.

Summary of outstanding ethical issues

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

* The Committee stated that the answer given to question P.2.7 of the application form did not reflect the question being asked, and asked for further information about how the research team would inform participants’ parents / caregivers of unexpected events that may occur during the study.
* The Committee stated that identifiable data should be destroyed 10 years after the youngest participant turns 16, however de-identified data could be kept indefinitely. Please clarify this in the protocol and associated documents.
* The Committee asked to see a data management plan, in accordance with standard 12.15a of the National Ethical Standards.

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

* Please mention that the research is being conducted in the hope of future commercial benefit and participants will not be eligible to claim financial benefit.
* Please use the ACC compensation template (within the HDEC PISCF template).
* Please provide more detailed information about what will happen with participants’ data, and how it will be kept confidential and private. Please refer to the HDEC PISCF template for guidance.
* Please consider increasing document margins, to improve ease of reading.
* Please ensure information is not repeated unnecessarily.
* Please mention in the PIS that participants may choose whether to have their information removed if they withdraw.
* Please use only one or two terms to refer to the infant.
* Consent form:
  + please delete the clause about blood samples.
  + Please delete the clause about maternal information, or if any information will be collected from the mother, make that clear in the PIS.

Decision

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

* Please outline how the research team would inform participants’ parents / caregivers of any unexpected events that may impact the decision to continue in the study.
* Please amend the information sheet and consent forms, taking into account the suggestions made by the committee
* Please submit a data management plan, in accordance with standard 12.15a of the National Ethical Standards.

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

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| **1** | **Ethics ref:** | **20/STH/123** |
|  | Title: | Morpheus study of new treatment combinations for advanced liver cancer |
|  | Principal Investigator: | Prof Ed Gane |
|  | Sponsor: | Covance New Zealand Limited |
|  | Clock Start Date: | 31 July 2020 |

Prof Ed Gane, Rebecca Hu, Eulyee Ahn, Rica Dagooc and Genevieve Morris were present via videoconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This is a phase Ib/II, open-label, randomised, 3-arm study of a new medicine and device for people with advanced liver cancer. It is planned as an "umbrella study" with more trial arms expected if new therapies/therapy combinations become available. The study will assess efficacy, safety and pharmacokinetics.
2. There are 2 stages in the study. Participants will be enrolled in stage 1 and randomly assigned to one of the 3 arms as below, with the likelihood of being allocated to the control arm to be <35%:
   * Control: atezolizumab + bevacizumab
   * Experimental: atezolizumab + bevacizumab + tiragolumab
   * Experimental: atezolizumab + bevacizumab + tocilizumab
3. Participants in Stage 1 who experience loss of clinical benefit or unacceptable toxicity may be given the option to be screened for Stage 2 as new treatments become available. Stage 2 of the study will be covered in a protocol amendment at a later time.
4. There is the option of using tissue for future unspecified research.
5. The study will involve approximately four participants in New Zealand.

Summary of resolved ethical issues

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

1. The Committee asked for an explanation of the relationship between the study medication and standard of care. The Researchers explained that the standard of care globally is sorafenib, however due to recent clinical studies showing the superiority of the combination of atezolizumab + bevacizumab has become the standard of care in the countries where it is registered and funded. In New Zealand there is no standard of care because even sorafenib is not funded. This study therefore will provide the best available treatment as the control arm. The experimental arm will provide the standard of care plus an additional treatment (the investigational agent PLN-74809).
2. The Committee asked whether archival tissue might be used in the study. The Researcher explained that it is not expected that archival tissue would be used for NZ participants.
3. The Committee asked about how de-identified information would be shared with the sponsor during the pre-screening stage. The Researchers clarified that no patient information will be shared with the sponsor at the pre-screening stage, only aggregate information about the study progression.
4. The Committee questioned whether information in the pre-screening PIS needs to be repeated in the main PIS. The Researchers explained that there is around a month delay between pre-screening and the signing of the main consent form.
5. The Committee noted that each participant information sheet/consent form was submitted to HDEC in duplicate.

Summary of outstanding ethical issues

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

1. The Committee asked for greater information on how data will be managed to ensure that the application complies with section 12.15.a of the National Ethics Standards.

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

1. Please proof-read the forms for formatting, typological errors, and repetition.
2. Please use reproductive risks template.
3. Participant should not need to ask for samples to be destroyed when withdrawing, as it is the researcher’s responsibility to check this with the participant at the time of withdrawal. Please amend accordingly in the relevant forms.
4. Please remove the yes/no tick boxes from the consent forms for all statements that aren’t truly optional, i.e. those where a participant could select ‘no’ and still participate in the study.
5. Main PIS and screening PIS: please clarify which genetic/biomarker assessments are mandatory and which are optional. Where optional, they should not be included in the main or screening PIS (i.e. whole genome testing should not be mandatory).
6. Main PIS:
   * “the following people and groups of people including people in other countries may look at your medical and personal information to …advance medical care and science”’ – please clarify whether that information is identifiable or de-identified, and amend to provide narrower reasons for access to identifiable information.
   * Please describe the risks of data linking.
   * Please state whether information used for FUR is mandatory or optional.
   * Consent form: please add a clause saying that the participant agrees to FUR.
7. Pregnant partner PIS: pregnant partners and infants are participants in research – please amend accordingly, and refer to HDEC partner pregnancy template for guidance.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the committee
* Please submit a data management plan, which explains the different aspects of data management outlined in standard 12.15a of the National Ethical Standards.

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

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| **4** | **Ethics ref:** | **20/STH/126** |
|  | Title: | Phase 1 Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of Novel Rifaximin Formulations in Healthy Volunteers |
|  | Principal Investigator: | Mr Christian Schwabe |
|  | Sponsor: | Novotech CRO |
|  | Clock Start Date: | 30 July 2020 |

Mr Christian Schwabe was present via videoconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This study is a phase 1, single-blind, randomised, placebo-controlled trial of three new rifaximin formulations in healthy adult participants. 108 participants will be enrolled in NZ only.
2. The study is an assessment of novel formulations of a previously approved medication involving single ascending dose (SAD) and multiple ascending dose (MAD) arms.
3. SAD: Participants are assigned to receive only one of the three formulations. For each formulation: 4 dose levels will be tested as single doses - 2 dose groups of 8; each participant gets 2-3 doses of study drug, with 7 days minimum between doses - Group 1 will get low dose + high dose +/- selected dose level (split into morning + evening doses) - Group 2 will get medium dose + maximum dose (split into morning + evening doses) - Dose levels will be enrolled in order, min 3 days between dose levels. 1 dose level will be tested as multiple doses - 1 dose group of 8; participants will receive study drug every day for 14 days. 1 dose level may be tested for food effect - 1 dose group of 12; participants get single dose fed and fasted in random order, with 7 days minimum between doses.

Summary of resolved ethical issues

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

1. The Committee noted that the ‘new formulations’ are considered new medicines, and it was confirmed that SCOTT review is underway.
2. The Committee noted that the dose-escalation will occur quite quickly, and asked if pharmacokinetic (PK) data would be available as part of the dose-escalation decision. The Researchers stated that there is very little systemic absorption expected, and the PK profile of the population is very well understood from previous studies. There is also an additional step between the single ascending dose and multiple ascending dose arms.
3. The Committee asked why there is sentinel dosing for the lowest dose, but not for other doses. The Researcher stated that this has been introduced as a precautionary step, but that sentinel dosing is not necessary in this study.
4. The Committee was satisfied that these issues will be reviewed by SCOTT.

Summary of outstanding ethical issues

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

1. The Committee asked for clarification as to whether there is only one level of randomization or two. Is a participant re-randomized at each different dose level?
2. The Committee asked to see a data management plan, in accordance with standard 12.15a of the National Ethical Standards.
3. Please amend the advertising material, removing the template language, correcting the title, and adding the number of overnight stays (and length of each stay) required for participants in the SAD arm.

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

1. Please add a lay title to each form.
2. Please proof-read for typographical errors and formatting.
3. Some sections of the PIS are repeated several times, please review and shorten where appropriate.
4. Main PIS (MD & SAD):
   * Please state the rates of adverse reactions.
   * Please ensure that all sections are completed (currently some are in template form).
   * Consent form: please add a yes/no option for receiving the study summary.
   * What does this study involve: Please clarify how many days in-house and how many clinic visits will be required for each arm.
   * Please explain the acronym “HbA1c”, and remove “(also called the aids virus)”
   * Right to access participant information: please clarify that while they have this right, if they do request to access non-safety / screening study information they may be unblinded and have to leave the study.
   * Reproductive risks section: condoms are not a highly effective form of contraception, please correct this. Please state whether there is any information about the reproductive risks of rifaximin.
5. MAD form: please submit as an amendment once the data is known from the single ascending dose arm.
6. SAD form:
   * please add information about the reduced dose BID investigation that cohort 1 would participate in. This could be clarified by separating the table between the cohorts.  
     The Researcher clarified that the study has three investigational parts, studying three formulations of the investigational product. Participants will be enrolled into the different formulation arms sequentially, depending on the timing. Please make this clear in the PIS.
   * Please correct the typo “indication” in the first sentence page 2.
7. Food effects PIS page 1: the study “may take place”, please correct.
8. Please note that the information under “what is your rights” is duplicated in the data section of the PIS, please amend accordingly.
9. Partner pregnancy PIS: please state whether there are any known reproductive risks of rifaximin.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the committee.
* Please submit a data management plan, which explains the different aspects of data management outlined in standard 12.15a of the National Ethical Standards.

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

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| **5** | **Ethics ref:** | **20/STH/124** |
|  | Title: | An effective point-of-care screening pathway for COVID-19 |
|  | Principal Investigator: | AP Jo Stanton |
|  | Sponsor: |  |
|  | Clock Start Date: | 30 July 2020 |

Assoc. Prof Jo-Ann Stanton was present via videoconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The purpose of the study is to test a new COVID-19 point-of-care device, and an associated screening pathway for primary care. The device and pathway will be trialled with a patient population over a 3-month period, recruited from community-based assessment centres and primary care practices. The purpose is validation of the technique against the current Ministry of Health standard laboratory testing. Individuals who visit a CBAC or supported primary care practice for assessment will be asked if they are willing to give an additional sample for processing through the investigational COVID-19 point of care pathway.
2. 300 participants will be recruited in NZ only.

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 how potential participants will be identified. The Researcher explained that people who have a COVID-19 screen will be identified by a GP at a COVID-19 screening station, and invited to undertake the additional screening procedure for this study.
2. It was clarified that the data in the study will be de-identified, rather than anonymous.
3. With regards to the possibility of incidental findings, the Committee asked what the Researchers’ approach would be if their test came out positive, but the standard of care test showed negative. The Researchers explained that they would act on the standard of care test (i.e. the study result would be considered a false-positive).
4. The Committee agreed that the information on data management provided was sufficient for this study.
5. The Committee noted that the study had undergone HRC review, and given the low risk was satisfied with this as evidence of scientific review.
6. The Committee questioned the number of participants and whether the current low rates of COVID-19 in the New Zealand population would reduce the ability of the study to assess sensitivity / specificity / predictive values with any reliability. The Researchers confirmed that this may be difficult, however the study would be very useful in terms of assessing feasibility and operational aspects of the test. if the results are promising, they would follow up with a larger study to assess test performance.
7. The Committee asked whether data from ESR for the bioinformatics for the test would need consent. The Researcher clarified that this is not a part of the present study, and would be part of a separate HDEC application.
8. The Committee asked for clarification if there is any potential for commercialisation of the device being validated in this study. The Researchers explained that while there is the potential for commercial benefit in the future, the present study is not sponsored by a commercial company and this is a very early proof of concept 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 asked to see a data management plan, in accordance with standard 12.15a of the National Ethical Standards. This can either be included in the study protocol or provided as a separate document.
2. Please add a statistical analysis plan to the study protocol.

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

1. Please give the form a lay title.
2. Please differentiate more clearly between the standard swab and the screening swab, to make it clear that participants will be given the result of the standard swab only.
3. The results of the swab are considered health information. Please state that you will not be collecting any *other* information.
4. If there is any potential for commercial benefit from this study, please explain this in the PIS.
5. Please state that the HRC is funding this study.
6. Page 3, rights to withdraw information: please ensure that this information is consistent with what is stated on the consent form.
7. Please add page numbers and a footer.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the committee.
* Please submit a data management plan, which explains the different aspects of data management outlined in standard 12.15a of the National Ethical Standards.
* Please add a statistical analysis plan to the study protocol.

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

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| **6** | **Ethics ref:** | **20/STH/125** |
|  | Title: | A study to test a new rectally administered drug for Ulcerative Colitis |
|  | Principal Investigator: | Dr Richard Stubbs |
|  | Sponsor: | Covance New Zealand Limited |
|  | Clock Start Date: | 30 July 2020 |

Dr Richard Stubbs was present via videoconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This will be an open-label, single-arm study of a new medicine for ulcerative colitis.
2. Eligible participants will receive the first dose of study drug at the study site on Day 1, following which study drug will be administered by participants once daily at home for 55 days After Day 1, participants will attend 5 study visits at the site.
3. The total duration of study participation for each participant (from screening through to follow-up visit) is anticipated to be approximately 99 days.

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 population number was sufficient to answer the study question. The Researcher explained that the study is primarily a proof of mechanism study, although signals of efficacy will be measured. Some exploratory outcomes will also be measured.   
   The proof of concept research has been done with the oral intake of this medicine, and this study is now testing a different mechanism.
2. It was confirmed that scientific review will be provided by SCOTT.
3. The Committee asked if participants should be given greater information about how the medicine will be administered, however the Researcher explained that this population will have had medication administered in this mode before.
4. The Committee asked about the deductibles on the insurance certificate, and the Researcher explained that the deductibles apply to the sponsor rather than to participants. It was further confirmed that the study will only be conducted in New Zealand.
5. The Committee asked where the endoscopies will be performed, because of the potential impact on public waiting lists. The Researcher explained that they will be performed at sites in Wellington and Tauranga at private clinics.
6. The Committee stated that health information needs to be retained for at least 10 years.
7. It was confirmed that participants will receive a separate, standard (not research-related) consent form for the endoscopy procedure.
8. The Committee noted the PISCF Flesch score of 90, and suggested that this may be an error.
9. The Committee noted that the questionnaires contain questions that could raise mental health concerns, and asked how participants’ answers will be monitored. The Researcher explained that the answers will be monitored by research staff as well as the data managers and CRO, and would be picked up quickly.

Summary of outstanding ethical issues

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

1. The Committee asked about the scope of access which the sponsor representatives would have to identifiable health records. The Researcher explained that only the sponsor’s monitors will be able to access identifiable information.   
   The Committee asked for this as well as other relevant information to be documented in a formal data management plan that covers the requirements in 12.15.a of the National Ethics Standards.

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

1. Please add a warning statement at the top of the first page saying that this is a first in human trial of this mode of administration.
2. Please explain gene expression, and what is being looked for in this study.
3. Table: please separate out the endoscopy visits, as these would occur at a different clinic.
4. Please make clear how much time participants will need to take out for the study visits.
5. Please state that test results for hepatitis B and C are notifiable to the director-general of health.
6. Gene expression, RNA analysis, and biomarker tests: please state what RNA is, and explain if this information could have any potential impact on the participant and their blood relatives. Please clarify the reason(s) for these tests e.g. for inflammatory markers.
7. Page 11: the statement “your samples will be made no longer available for tests and will be destroyed” is inconsistent with the earlier statement on page 5 “any samples collected up to your point of withdrawal will be retained and still be used”. Please amend for consistency.
8. Page 11 data section: please add information about data risks, ownership of data, return of study results and incidental findings. Please state clearly if data may be used for future related or unrelated research.
9. Please add a statement about cultural considerations regarding the use of tissue.
10. Please remove all the non-optional “yes” boxes on the PIS.
11. Page 3: please make clear that no DNA/RNA testing will be conducted other than that specified in the form.
12. Page 2: please amend “this study has received favourable opinion from the ethics committee” to “has been approved…”

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the committee.
* Please submit a data management plan, which explains the different aspects of data management outlined in standard 12.15a of the National Ethical Standards.

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

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| **7** | **Ethics ref:** | **20/STH/119** |
|  | Title: | (duplicate) RESOLVE |
|  | Principal Investigator: | Dr Mark Marshall |
|  | Sponsor: |  |
|  | Clock Start Date: | 09 July 2020 |

Dr Mark Marshall was present via videoconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This is a pragmatic, cluster-randomised, open-label trial to evaluate the relative effectiveness of two different default dialysate sodium concentrations on cardiovascular events and mortality among dialysis patients. Dialysis facility sites will be randomised to use either 137mmol/l or 140mmol/l of dialysate sodium concentration for their patients, and outcomes will be assessed on individual patients dialysing in those sites. Sites will be asked to consent to participation, and simplified opt-out consent will be sought for individual patients. The trial design allows the evaluation of health service practice by assessing efficacy in all patients who are exposed to default dialysate sodium, including the sicker and more vulnerable patients who typically do not participate in individually randomised opt-in trials.
2. The aim of this global study is to establish whether treatment with a default dialysate sodium concentration (of 137 mmol/l compared with 140mmol/l) reduces major cardiovascular events and death in adult patients receiving haemodialysis in centres employing a default dialysate sodium.
3. An application for this study (18/STH/164) was originally approved by the Southern HDEC with a waiver of consent, however subsequently that approval was withdrawn following a determination that a waiver of consent was not legal, as the study was providing an intervention. As written consent from participants is not feasible for a cluster-randomized design, this new application is updated with an opt-out consent model.

Summary of outstanding ethical issues

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

1. The Committee noted that it could only approve a trial that was in accordance with New Zealand law, and while the Researchers had provided a legal opinion asserting that the trial was in accordance with New Zealand law, a second legal opinion was provided by Health Legal.
2. The Committee was ultimately more persuaded by the opinion from Health Legal, and was not satisfied that the trial would be legal so long as written consent is not sought from the trial participants.
3. The Researcher asked for advice on how the trial could proceed, and noted that to seek written consent from all participants would be both less scientifically rigorous and unethical. The Committee stated that it was not satisfied that this study would be possible unless there is a change to New Zealand law.

Decision

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

1. Researchers must be able to justify an opt-out approach by ensuring that (among other conditions) the opt-out approach is not prohibited by law (*National Ethics Standards* para *7.45*). The Committee was not satisfied that the opt-out approach proposed would be in accordance with New Zealand law. In particular, it appears that it would contravene Right 7(1) and (6) of the Code of Health and Disability Services Consumers’ Rights 1996.

Furthermore, it is not clear that:

* + the Committee has any power to waive the requirements of the Code other than where an exception to that right is set out in the Code itself or in any other law;
  + there is an exception to the requirement for written informed consent to participation in research under right 7(1) or 7(6) which would apply to this kind of study (other than where a particular participant was not competent to consent and the requirements of Right 7(4) had been met);
  + consent is not required for participation in research where specific consent to treatment is not necessary for a procedure that forms part of the research;
  + the Health Information Privacy Code would remove the need for informed consent to participation in the study at the point when treatment was provided.

## General business

1. The Committee noted the content of the “noting section” of the agenda.
2. The Chair confirmed that a meeting with the Chair of SCOTT had been arranged, to take place prior to the next full Southern meeting, to discuss the role of SCOTT in conjunction to the HDECs.
3. The Chair reminded the Committee of the date and time of its next scheduled meeting, namely:

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| --- | --- |
| **Meeting date:** | 08 September 2020 |
| **Meeting venue:** | Via videoconference |

1. **Review of Last Minutes**

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

The meeting closed at 3:10pm.