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| **Committee:** | Southern Health and Disability Ethics Committee |
| **Meeting date:** | 12 February 2019 |
| **Meeting venue:** | Sudima Hotel, Christchurch Airport, 550 Memorial Drive, Christchurch |

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| **Time** | **Item of business** |
| 11:30am | Welcome |
| 11:35am | Confirmation of minutes of meeting of 29 January 2019 |
| 11:40am  11:45am | General business   * Noting section   New applications (see over for details) |
| 11:45 – 12:10pm  12:10 – 12:35  12:35 -1:00  1:00 – 1:25  1:25 – 1:50  1:50 – 2:15  2:15 – 2:40 | i 19/STH/31 (Raewyn/Sarah)  ii 19/STH/32 (Helen/Devonie)  iii 19/STH/41(Raewyn/Paul)  iv 19/STH/40 (Helen/Mira)  v 19/STH/36 (Raewyn/Nicola)  vi 18/STH/164 (Raewyn/Sarah)  vii 19/STH/42 (Helen/Mira) (CLOSED) |
| 2:40 – 2:45pm | Review of approved studies (see over for details) |
| 2:45 – 2:50pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |  |
| Ms Raewyn Idoine | Lay (consumer/community perspectives) | 27/10/2015 | 27/10/2018 | Present |  |
| Dr Sarah Gunningham | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | Present |  |
| Assc Prof Nicola Swain | Non-lay (observational studies) | 27/10/2015 | 27/10/2018 | Present |  |
| Dr Devonie Waaka | Non-lay (intervention studies) | 13/05/2016 | 13/05/2019 | Present |  |
| Assc Prof Mira Harrison-Woolrych | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | 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 | Apologies |  |
| Mrs Helen Walker | Lay (consumer/community perspectives) | 01/07/2015 | 01/07/2018 | Present |  |

## Welcome

The Chair opened the meeting at 11:30am and welcomed Committee members, noting that apologies had been received from Professor Jean Hay-Smith.

The Chair noted that it would be necessary to co-opt members of other HDECs in accordance with the Standard Operating Procedures. Mrs Helen Walker confirmed her eligibility, and was co-opted by the Chair as a member of the Committee for the duration of the meeting.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

## Confirmation of previous minutes

The minutes of the meeting of 29 January were confirmed.

## New applications

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| **1** | **Ethics ref:** | **19/STH/31** |  |
|  | Title: | ABI-H0731-211: A Long-term Extension Study of ABI-H0731 + Nucleos(t)ide as Finite Treatment for Chronic Hepatitis B Patients |  |
|  | Principal Investigator: | Prof Edward Gane |  |
|  | Sponsor: | Pharmaceutical Research Associates Ltd (NZ) |  |
|  | Clock Start Date: | 25 January 2019 |  |

Prof Edward Gane and Ms Chin Kuh were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The study drug ABI-H0731 is being developed as a potential new treatment for Chronic Hepatitis B (CHB) virus infection (HBV). It works by inhibiting hepatitis B virus replication and preventing the virus from making its inner coat which is essential for many steps of the hepatitis B virus lifecycle.
2. This is the first phase 2, extension-phase study, for people who have been participating in 2 studies in which they received ABI-H0731 once daily for 24 weeks. In this study they will be offered treatment up to 54 weeks, depending on their response. After 24 weeks their on-treatment response is determined. If they are non-responsive to the drug, treatment will stop. If they are responsive, then will continue until 54 weeks, or until the hepatitis B virus is completely eradicated.
3. There is only one patient 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 stated for future reference, that in answering question r.1.1 of the application form, it would be useful to have a summary of the study drug risks.
2. The Committee queried whether the participant will have continued access to the treatment after the end of the study if required. The Researcher clarified that participants who are not complete responders will continue to receive the standard of care medicine, which his cheaply available from Pharmac, not ABI-H0731.

Summary of outstanding ethical issues

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

1. In the application form, at question p.2.7, the Researcher stated that the site will await approval of an updated ICF before informing participants of new information that may impact on them. The Committee requested that the Researcher ensure that if this pertains to significant new risk information that may affect a participant's decision to stay in the study, participants are informed *prior* to the development and approval of an updated ICF document.

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

1. Please increasing the spacing for legibility.
2. Please remove any duplicated information.
3. The section on reimbursement for the study is blank. Please submit this as an amendment to the study once the sponsor has confirmed it.
4. Please remove the section where it states that notification to revoke consent needs to be in writing.
5. A separate pregnancy-consent form is required for once the baby is born. Please contact Nic Aagaard in the Secretariat if you require the legal opinion regarding this.
6. Please amend the title to make it suitable for lay readers. The Committee suggested “ABI-H0731 as a treatment for chronic Hepatitis B patients”.
7. Please correct the definition of ‘open label’ in sections 1 and 3.
8. On page 2, please change “you’ve been asked to participate because you have CHB in one or more of the following conditions” to “you’ve been asked to participate because you have CHB in one or more of the following”.

Decision

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

1. Please amend the protocol to ensure that participants are informed of any significant new risk information that may affect their decision to stay in the study prior to the development and approval of an updated PIS/CF document (*Ethical Guidelines for Intervention Studies* paragraph 6.21).
2. Please submit the section on reimbursement for the as an amendment once the sponsor has confirmed it (*Ethical Guidelines for Intervention Studies* paragraph 6.36).
3. Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* paragraph 6.22).

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| **2** | **Ethics ref:** | **19/STH/32** |  |
|  | Title: | KEYNOTE-913 |  |
|  | Principal Investigator: | Dr Ben Lawrence |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 31 January 2019 |  |

This application was *approved.*

**CLOSED MINUTES**

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| **3** | **Ethics ref:** | **19/STH/41** |  |
|  | Title: | Phase 1b study to determine the safety, tolerability and pharmacokinetics of RTB101 and sirolimus alone or in combination in patients with Parkinson's Disease. |  |
|  | Principal Investigator: | Prof Tim Anderson |  |
|  | Sponsor: | Pharmaceutical Solutions Ltd |  |
|  | Clock Start Date: | 31 January 2019 |  |

Prof Tim Anderson, Kerry Russell, Karen Jauregui, and Sarb Shergill were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The study investigates a new treatment for Parkinson’s disease. The study treatments are sirolimus and RTB101, administered separately and in combination. Neither sirolimus nor RTB101 have been tested in PD patients. The Researchers believe there is a lot of pre-clinical data that mTOR inhibitors would have a significant impact on neuro-degenerative disorders, including parkinsons.

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 what would be done if a participant refuses the LP procedure, or if the LP procedure fails for technical reasons. The Researchers responded that in both cases the participant would be withdrawn from the study.
2. The Committee queried whether the Researchers plan to do sentinel dosing, as this is the first in-human trial with this combination of drugs. The Researcher stated that they have not planned to do so, in particular because a similar drug combination has already been tested in patients.
3. For future reference, the Committee stated that it would have been useful in answering question p.4.1 of the application form to have stated the statistics of Parkinson’s disease in Maori.

Summary of outstanding ethical issues

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

1. The Committee asked what safety plan is in place in the event that a participant’s answers on the Colombia indication questionnaire indicate that they are distressed or suicidal. The Researchers replied that if the score indicates that the person is suicidal they will be referred to a psychiatrist. The Committee requested that this be included in the study protocol, detailing what responses would prompt action, what the action will involve and how patients may be monitored.
2. There was an inconsistency in the Researchers’ answers in the application form regarding whether samples will be used for future unspecified research or not. The Committee asked for clarification, and the Researchers explained that although samples will not be used for unspecified research, they may be used for a specific future sub-study. The Committee noted, however, that the future research is not specified in the PIS, and therefore remains unspecified for the participant. As the Researchers did not answer the appropriate questions in the application form regarding future unspecified research, the Committee stated that any future sub-study would need to be reviewed before the study could be fully approved.

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

1. Please add a warning box at the beginning of the PIS, stating that this is the first-in-human test of this combination of drugs, such as “Although the study drugs have been tested in humans before, this is the first time the combination of these drugs will be studied. You may not receive any health benefit from the study drugs; but there are risks of you having a drug reaction, injury or illness’.
2. In the section on the risks of this study, please describe in how many human subjects these drugs have been trialled.
3. In the section on the risks of this study, please explain the term “lympho-proliferative disorders”, making it appropriate for lay readers.
4. In the section titled “what will happen to information about me”, it states that the patient’s identity will be kept confidential by only using an assigned study number, and then states that the patient’s records are subject to inspection by several people. Please specify the circumstances where identifiable information will be accessed by these groups.
5. The Committee noted some inconsistencies between the application form and the PIS, for example regarding whether tissue samples will be sent overseas or not. Additionally, it noted the PIS does not explain what will happen with CSF samples. Please make sure these points are consistent and proof-read for other inconsistencies.
6. Please state, regarding the future use of samples, whether genetic testing will be carried out or not.
7. Please ensure that the font size is consistent throughout the document.
8. Please ensure text is properly aligned on the first page, and move the address details of the sponsors to the end of the document.

Decision

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

* Please clarify whether tissue samples will be used for future research by answering the following questions (*Standard Operating Procedures for Health and Disability Ethics Committees* paragraph 42.3):
* b.4.5.1. Will consent for future unspecified use of human tissue be obtained separately from consent to participate in your study? (yes/no)
* b.4.5.2. Please briefly describe the possible future uses for human tissue collected in your study.
* b.4.5.3. Will any human tissue collected or otherwise obtained from participants in this study but not used in it be stored or sent overseas? (yes/no)

Please include your answers in the provisional approval response letter.

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* paragraph 6.22).

This following information will be reviewed, and a final decision made on the application, by Ms Raewyn Iodine and Dr Paul Chin.

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| **4** | **Ethics ref:** | **19/STH/40** |  |
|  | Title: | Comparison of the blood levels of a combination tablet containing paracetamol/ibuprofen/doxylamine and a combination tablet containing paracetamol/codeine/doxylamine in healthy volunteers. |  |
|  | Principal Investigator: | Dr Noelyn Hung |  |
|  | Sponsor: | Soul Pattinson (Manufacturing) Pty Ltd (SPM) |  |
|  | Clock Start Date: | 31 January 2019 |  |

Dr Noelyn Hung 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. A phase 1 bioequivalence study in 24 volunteers of two painkiller medications.

Summary of outstanding ethical issues

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

1. The Committee observed that the participants in this study are likely to be students, and therefore vulnerable to monetary incentives. Consequently, it stated that further care needs to be made to make them aware of the study risks.

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

1. Please simplify the study title, making it appropriate for lay readers.
2. The Committee stated that bleeding is a possible side-effect of ibuprofein, but was not included in the PIS. The Researcher clarified that they will exclude patients who are susceptible to bleeding. The Committee stated that this needs to be listed in the exclusion criteria.
3. Under “what are the possible benefits and risks of this study?” on page 6, please describe the full list of potential adverse effects of each of the medicines. Please state the frequencies of participants in which those adverse effects are observed. The Committee suggested that the Researcher use the MedSafe data sheet to group the risks of each active medicine and insert that into the PIS in lay language.
4. Please describe the possible risks of drowsiness or sedation, and state whether the participant should expect those effects to be an issue by the time they leave the study site.
5. Please include information on what action you will take in the case that patients experience adverse reactions after they leave the study site.
6. Under “what are the possible benefits and risks of this study?” on page 6, any reproductive risks need to be outlined. Please amend this, noting that abstinence has been shown not to be an effective form of contraception. The Committee suggested that the Researcher use the HDEC template when editing this section.
7. In the same section, please state for how long you want participants to use contraception for.
8. Please edit the PIS, removing any terms which lay people might struggle to understand.
9. Please add space between paragraphs and wider margins to improve readability.
10. On page 9, in the first paragraph it states that blood and plasma samples are going to be sent away for testing and disposed of, as well as retained for a year. Please correct this inconsistency.
11. In the advertisement document, the drug combinations listed in the first paragraph are identical. Please correct this.

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* paragraph 6.22).

This following information will be reviewed, and a final decision made on the application, by Mrs Helen Walkder and Ass Prof Mira Harrison-Woolrych.

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| **5** | **Ethics ref:** | **19/STH/36** |  |
|  | Title: | Evaluating the IR experiences of young people in hospital |  |
|  | Principal Investigator: | Dr Hiran Thabrew |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 31 January 2019 |  |

No member of the research team was 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 study aims to: 1) quantitatively evaluate the effectiveness of IRE technology in improving wellbeing, social connectedness and social inclusion; and 2) explore participants’ and their family’s or school staff’s views related to social inclusion, social connectedness and wellbeing.
2. Young people with any medical condition, aged between 13-18 years and admitted to Starship Hospital for more than a 2-week period or intermittently over a longer period will be eligible to participate in the study. Following pre-intervention measures, participants will have access to IRE technology for 6 weeks, at the end of which they will complete post-intervention measures and be invited to participate in semi-structured interviews alongside consenting family and school staff.

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 issue of privacy with other students and the teacher in the class. It stated that as those other children and adults are being monitored, they should consent to their participation.
2. One of the three scales, the short SCOPE, does not seem appropriate for young people e.g. asks about main source of income. Please either justify its use, or find an equivalent scale for use in young people. Further, the scale asks “have you been a victim of a crime or assault”. There should be an explicit plan in the protocol for managing “Yes” answers to this question.
3. As a whole document, the protocol is not extensive enough. More specifically, the following aspects of the protocol require changing:
   * No specific exclusion or inclusion criteria have been included
   * There is inadequate information on the previous stage of the trial, such as who it was approved by.
   * There is no information on confidentiality issues concerning school students being filmed.
   * The data storage plan is inappropriate.

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

1. The PIS for participants under 16 years of age contains language that is inappropriate for persons of that age.
2. Please remove the SCOPE questionnaires (unless justified).
3. Please remove the question regarding whether “you’ve been a victim of assault” from the questionnaire.
4. Please clarify the method of participant identification (will a pseudonym or a study code be used?).
5. Please clarify what will happen if the participant pulls out of the study, i.e. will their data will be withdrawn?
6. Please edit the PIS documents to use language appropriate for a lay audience.
7. Please proofread the PIS documents, removing any incorrect statements e.g. “no information about you will be collected”.
8. The Committee recommends that the research office be involved in assisting with age-appropriate PIS sheets.

Decision

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

* *Ethical Guidelines for Intervention Studies* paragraph 6.22
* *Ethical Guidelines for Intervention Studies* paragraph 7.11
* *Ethical Guidelines for Intervention Studies* paragraph 5.41

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| **6** | **Ethics ref:** | **19/STH/42** |  |
|  | Title: | A Phase 3 Study of Pemetrexed + Platinum Chemotherapy + Pembrolizumab with or without Lenvatinib in Participants with NSCLC |  |
|  | Principal Investigator: | Dr Richard North |  |
|  | Sponsor: | MSD |  |
|  | Clock Start Date: | 31 January 2019 |  |

**CLOSED MINUTES**

## Substantial amendments

## Review of approved studies

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| **1** | **Ethics ref:** | **18/STH/164** |
|  | Title: | RESOLVE |
|  | Principal Investigator: | Dr Mark Marshall |
|  | Sponsor: |  |
|  | Clock Start Date: | 02 August 2018 |

Dr Mark Marshall 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. Dialysis is used for renal failure and prolongs life from a matter of weeks to months to a matter of months to years. There are numerous technical variations in dialysis and these can be manipulated to meet the wishes and medical needs of patients. The concentration of sodium in dialysate is one such variable. A range of sodium concentrations are used worldwide. In New Zealand dialysis units use concentrations ranging from 136 -141 mmol/L. The concentration used in each unit is determined largely by customary practice, habit, history and occasionally biomedical need.
2. This study aims to see whether sodium dialysate concentration affects cardiovascular outcomes in dialysis patients. The study will cluster randomise 400 dialysis units around the world, including 15 units in New Zealand, to one of two sodium dialysate concentrations. Both concentrations are widely used in New Zealand and overseas, and fall within the range currently used by New Zealand sites.
3. The Secretariat explained that this study was brought back to the Committee to clarify that it was an intervention study involving randomisation. It was initially approved as an observational study that only sought to access health information through a waiver of consent to health data. The Researcher confirmed that it was an intervention study that involved cluster randomisation, and that it was designed to not seek individual informed consent.

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 and the researcher discussed the study, different consent options and its ethical review and approval in other countries. The Committee noted that their role is not to provide a legal opinion, but in cases where the legality of a study was in question they were able to seek their own legal advice, or have the researchers seek legal advice.
2. Although the Committee had no ethical issues with the study, it noted that, as a cluster randomized trial that was designed not to seek individual informed consent. It observed that this is an area where the law is not clear. Due to this legal ambiguity the Committee noted that they could not approve the study without evidence that the study met legal requirements for informed consent in New Zealand.
3. The Committee observed that there are no risks to participants associated with the study beyond what they would be exposed to by the standard of care, and that the study has the potential to be greatly beneficial for New Zealanders.
4. The Committee noted if the researcher could provide a legal opinion that explained how the study met New Zealand law they would reconsider their decision, reiterating that they had no ethical issues with the study and recognised its social value and low risk of harm.
5. The Committee noted that this type of research should be conducted in New Zealand and would be happy to write a letter to the researcher in support of the study in order to find a solution to what the Committee view as a legal barrier to ethical research in New Zealand.

Decision

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

* *Ethical Guidelines for Intervention Studies* paragraph 6.26.

## 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:** | 12 March 2019 |
| **Meeting venue:** | Sudima Hotel, Christchurch Airport, 550 Memorial Drive, Christchurch |

1. **Problem with Last Minutes**

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

The meeting closed at 2:45pm.