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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 15 November 2016 |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

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| **Time** | **Item of business** |
| 1:00pm | Welcome |
| 1.05pm  1.10pm | Confirmation of minutes of meeting of 11 October 2016  General Business  Noting Section of agenda |
| 1:30pm | New applications (see over for details) |
|  | i 16/NTA/188  ii 16/NTA/194  iii 16/NTA/177  iv 16/NTA/179  v 16/NTA/180  vi 16/NTA/181  vii 16/NTA/178  viii 16/NTA/190  ix 16/NTA/184  x 16/NTA/183  xi 16/NTA/192 |
| 6.05pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Brian Fergus | Lay (consumer/community perspectives) | 11/11/2015 | 11/11/2018 | Present |
| Dr Karen Bartholomew | Non-lay (intervention studies) | 13/05/2016 | 13/05/2019 | Present |
| Dr Christine Crooks | Non-lay (intervention studies) | 11/11/2015 | 11/11/2018 | Present |
| Dr Kate Parker | Non-lay (observational studies) | 11/11/2015 | 11/11/2018 | Present |
| Dr Charis Brown | Non-lay (observational studies) | 11/11/2015 | 11/11/2018 | Present |
| Ms Rosemary Abbott | Lay (the law) | 15/03/2016 | 15/03/2019 | Present |
| Dr Catherine Jackson | Non-lay (health/disability service provision) | 11/11/2016 | 11/11/2019 | Apologies |
| Ms Toni Millar | Lay (consumer/community perspectives) | 11/11/2016 | 11/11/2019 | Present |

## Welcome

The Chair opened the meeting at 1pm and welcomed Committee members, noting that apologies had been received from Dr Catherin Jackson.

The Chair noted that Ms Toni Millar was attending in an observational capacity and was not reviewing 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 October were confirmed.

## New applications

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| **1** | **Ethics ref:** | **16/NTA/188** |
|  | Title: | A study of RO7062931 in healthy subjects and patients chronically infected with hepatitis B virus infection |
|  | Principal Investigator: | Professor Ed Gane |
|  | Sponsor: | Covance NZ Ltd |
|  | Clock Start Date: | 03 November 2016 |

Dr Paul Hamilton and Ms Mary Ellis-Peglar were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The study is a phase I clinical trial of the study drug, RO7062931, to test its’ safety and tolerability in human subjects.
2. The Committee noted that that the study protocol is an umbrella protocol.
3. The drug is administered subcutaneously and the researchers aim to recruit 80 participants in this trial.

Summary of ethical issues (resolved)

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

1. The Committee queried how long the first phase of the study takes. The researchers explained that the first phase takes 29 days. The first three days are in-house and there are 6 follow up visits up to the 29th day endpoint.
2. The Committee queried how long the analysis of the results from the first phase will take. The researchers explained that they will be holding meetings to discuss the findings before moving onto the second phase.
3. The Committee noted that after part I they would like to see the new participant information sheet (PIS) that reflects any changes.
4. The Committee queried the likelihood of the risks mentioned in the PIS. The researchers explained that as this is a first in human trial they cannot provide a likelihood of these outcomes. The researchers explained that they take the safety of participants very seriously and referred to their study protocol’s section on safety.
5. The Committee queried if biomarker testing was mandatory. The researchers explained that it is and that sample will be stored for two years.
6. The Committee noted that the future unspecified research (FUR) consent form seeks blanket consent (allowing study of “any broad health question”) and asked if this was the researcher’s intent. The researchers explained that it was.
7. The Committee queried if the researchers had heard from SCOTT. The researchers stated that they had not.
8. The Committee clarified that the second phase of the study would need to be submitted as an amendment to be reviewed by the full committee.
9. The Committee asked why they are studying in healthy volunteers and patients with chronic hepatitis b at the same time. The researchers explained that this was being done in order to make the study process faster and that it helps improve their understanding of the pharmacokinetics of the study drug.

Summary of ethical issues (outstanding)

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

1. The Committee queried the length of time of storage for FUR samples, and where they would be stored. The researchers explained that samples would be retained for 15 years in a laboratory in Switzerland. The committee requested that these details be included in the PIS, along with the address of the laboratory.

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

1. Please revise PIS for the use of jargon (eg “sentinel dosing”) and localise the PIS to use New Zealand terminology as some of the phrasing could be considered United States-centric, including use of the word ‘race’ (page 6).
2. The Committee noted that the three sections on confidentiality are confusing (PIS pages 17-18). Please amend these into a single section and clearly clarify the wording around the disclosure of health information, and whether or not the information disclosed will be identifiable or not. Current wording appears to request permission for identifiable data to be released to the sponsor which the Committee does not support.
3. Please remove the statement in the benefits section around phase one studies being necessary. The Committee felt that this was potentially coercive.
4. Please add the duration of storage for FUR samples and the address of the laboratory in Switzerland where samples will be stored.
5. Please remove the statement about legal representatives providing consent (PIS 2, page 18).

Decision

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

* Please provide the outcome of SCOTT review. (*Ethical Guidelines for Intervention Studies* Appendix 1).
* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).

This following information will be reviewed, and a final decision made on the application, by Dr Brian Fergus and Dr Karen Bartholomew.

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| **2** | **Ethics ref:** | **16/NTA/194** |
|  | Title: | GALACTIC-HF |
|  | Principal Investigator: | Professor Russell Scott |
|  | Sponsor: |  |
|  | Clock Start Date: | 03 November 2016 |

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

Potential conflicts of interest

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

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

Summary of Study

1. The study is a cardio vascular disease endpoint study. The aim is to see if it is possible to reduce heart failure hospitalisations or death for those with low ejection fractions.
2. The study is a phase III study and involves eight thousand participants across 7 countries. 35 participants across three sites in New Zealand will be recruited. NZ will be the first to gain ethics approval.
3. The study is projected to take four years to complete.
4. The researcher explained that they have multiple potential endpoints as the study is powered to stop once there are 20% of the study population with secondary endpoints.
5. All participants will have class two to class four heart failure.
6. Recruitment will be done through hospitals and primary care providers. There will also be online advertising. Patients with comorbidities will be excluded.

Summary of ethical issues (resolved)

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

1. The Committee queried how recruitment and selection occurs. The researchers explained that they will have an experienced nurse who has received training to identify potential participants. These will be identified through the hospital’s system. The researchers will also individuals who they are familiar with from their previous studies.

Summary of ethical issues (outstanding)

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

1. The Committee stated that the recruitment procedures could be considered coercive (particularly for patients in hospital with acute health failure) and request further information about the recruitment process and how potential coercion will be managed.
2. The Committee noted that the recruitment process needs to be included in the participant information sheet. Please include why participants have been approached.
3. The Committee noted that page 16 of the information sheet could imply that the study will be stopped for purely commercial reasons. HDECs do not support this. Please provide the reasons why the study might be stopped and include these in the information sheet.
4. The Committee noted the IB states a phase II trial is still running and asked why this phase III trial had started. The researcher advised they would clarify with the sponsor whether any safety concerns from the phase II trial could affect participants in this trial.
5. The Committee queried if the active drug would be made available to participants at the end of the study if it is shown to be beneficial. The researcher explained that there would not. Please include this in the participant information sheet.
6. The Committee noted that the application a.1.5 states that the dose of the study drug may be adjusted in the study, and queried how this would be possible if the study is blinded?

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

1. Please review the PIS for typos, jargon and repetition.
2. Add why participants have been approached about study participation.
3. Please ensure that the participant information sheet and consent form’s language has been suitably localised to a New Zealand setting eg medical benefits.
4. Please clearly explain the criteria for study termination.
5. Please remove the statement on page three about participants needing to continue taking the drug (from “The quality of the study will be best if all patients continue taking study drug…” This is a coercive statement and participants must feel free to withdraw if they wish.
6. Please add a statement that the active drug will not be made available to those taking the placebo at the end of the study if the drug is found to be beneficial.
7. Please amend the information sheet to clearly state that no identifiable health information will be disclosed. Only de-identified health information.
8. Please check the sections on confidentiality and privacy for accuracy and clarity.
9. Please add explanations for why procedures such as blood tests need to take place (what kind of blood tests will be taken in lay language). Do not refer participants to the study protocol (page 6), this section needs revision.
10. Please combine your information sheets and consent forms for genomic analysis and future unspecified research into a single form (the purpose of a separate consent is to clearly distinguish that future unspecified use testing is optional and what it involves (genetic and other tests). Please refer to the Future Unspecified Use guidelines and ensure that the required information is included.
11. Please include information and consent for follow up of participants longer term (or until death) in lay language.
12. Please clarify where the samples will be stored – page 4 says Australia, US, Europe and Said for 15 years and elsewhere it states for 20 years and only in Singapore. Please clarify. Both the main study and the future unspecified use PIS need to state length of time of storage and where samples will be stored.
13. Please note the future unspecified research appears to be requiring additional blood samples (taken at the time of other samples) not just leftover blood, please note this.
14. Please add an area code for the Māori contact person.
15. Please remove the statement about an HDEC-approved auditor from the consent form.

Decision

This application was *provisionally approved* by consensus, 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* *para 6.22*).
* Please explain what procedures are in place to manage the potential coercion in the recruitment process.
* Please confirm that the study will not be terminated purely for commercial reasons.

This following information will be reviewed, and a final decision made on the application, by Ms Rosemary Abbott and Dr Christine Crooks.

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| **3** | **Ethics ref:** | **16/NTA/177** |
|  | Title: | ICU-ROX TRIPS |
|  | Principal Investigator: | Ms Diane Mackle |
|  | Sponsor: | Medical Research Institute of NZ |
|  | Clock Start Date: | 28 October 2016 |

Dr Paul Young and Ms Diane Mackle were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This study seeks to determine if healthcare professionals participating in the ICU ROX study will change their practice and attitudes to oxygen management in an observable way, regardless of the ICU ROX study outcomes. The second aim is to detect if a significant difference in favour of a more conservative oxygen therapy model then it will occur in participating units, rather than in non-participating units, or those outside Australia and New Zealand.
2. The Committee sought clarification on what part of the study they should be reviewing as the documents provided were not clear. The researchers explained that they would like the Committee to examine the retrospective review of data and the prospective observational (Inception Cohort) study. The health professional survey had been reviewed and approved by an Institutional Committee.
3. The prospective observational study involves the recording of oxygen levels and other routinely collected data from ICU patients in order to determine current practice before and after the ICU ROX study (one sites will not be involved in ICU ROX). Consent will not be sought prospectively or retrospectively.
4. The retrospective review uses data drawn from an international clinical database that is fully anonymous.
5. The researchers explained that they want to see how ICU units respond to ICU ROX staff training.
6. The researchers stated that this study is observational research and not an audit, as it can be generalised across intensive care units and isn’t looking at an improvement of service as its’ primary outcome.

Summary of ethical issues (resolved)

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

1. The Committee asked if the details required for the prospective analysis is contained in the hospital registries. The researchers explained that it is not as it is more detailed than the information in the registries (information from patient clinical notes).
2. The Committee asked if the details required for the prospective analysis is contained in the hospital registries. The researchers explained that it is not as it is more detailed than the information in the registries.
3. The Committee noted that the observational part of the study should be considered prospective.
4. The Committee asked the about the process of linking the datasets in the retrospective part of the study. The researchers explained that the data will be drawn from the ANZICS database and is fully anonymous.

Summary of ethical issues (outstanding)

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

1. The Committee stated that it is not possible for HDECs to approve an application unless it is consistent with New Zealand law, including the right not to be subjected to medical or scientific experimentation without that person's consent (section 10 of the New Zealand Bill of Rights Act 1990). Research involving participants who are not competent to consent is inconsistent with the Bill of Rights unless it is undertaken in accordance with Right 7 (4) of the of the Code of Health and Disability Services Consumers’ Rights. In addition to requirements regarding ascertaining the views of the consumer and other suitable persons (forms consistent with this aspect are currently included in this application), Right 7(4) of the Code requires that any health services provided without the informed consent of the consumer must be in the best interests of the consumer. This means that there must be some benefit, or potential benefit, to the participant beyond what they would receive if they were not participating in the research. Please provide evidence that participation in this study will not conflict with Right 7.4.

Decision

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

* The Committee understands that information recorded accessed in the prospective part of the study will be beyond that collected as part of standard care. The Committee stated that it is not possible for HDECs to approve an application unless it is consistent with New Zealand law, including the right not to be subjected to medical or scientific experimentation without that person's consent (section 10 of the New Zealand Bill of Rights Act 1990). Research involving participants who are not competent to consent is inconsistent with the Bill of Rights unless it is undertaken in accordance with Right 7 (4) of the of the Code of Health and Disability Services Consumers’ Rights. In addition to requirements regarding ascertaining the views of the consumer and other suitable persons (forms consistent with this aspect are currently included in this application), Right 7(4) of the Code requires that any health services provided without the informed consent of the consumer must be in the best interests of the consumer. This means that there must be some benefit, or potential benefit, to the participant beyond what they would receive if they were not participating in the research. If data collected in this study will be beyond that collected as part of standard care is the case please provide evidence that participation in this study will not conflict with the Right 7.4 requirements. If information collected will only be equivalent to that collected as part of standard care then please notify the Committee of this.

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

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| **4** | **Ethics ref:** | **16/NTA/179** |
|  | Title: | Study of safety, tolerability, pharmacokinetics and efficacy of LMB763 in patients with non-alcoholic steatohepatitis (NASH) |
|  | Principal Investigator: | Dr Dean Quinn |
|  | Sponsor: | Novartis Institutes for Biomedical Research |
|  | Clock Start Date: | 03 November 2016 |

Dr Dean Quinn 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 assesses the safety, tolerability, efficacy, and pharmacokinetics of the study drug LMB763.
2. The study aims to recruit 96 people (potentially up to 200 people), with 25 in New Zealand and 100 in the United States.
3. The study has received ethics approval in the United States.

Summary of ethical issues (resolved)

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

1. The Committee stated that the Health Information Privacy Code requires that participants be able to access their information on request. The research explained that participants are free to do this but it will result in their withdrawal from the trial.
2. The Committee queried who the ‘certain organisations’ are that will have access to data. The researcher explained that the data will be restricted to research teams only.

Summary of ethical issues (outstanding)

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

1. The Committee asked about the peer review for the study. The researcher explained that they had sent the study to the Standing Committee on Therapeutic Trials (SCOTT.)

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

1. The Committee queried the definition of personal data. The researcher explained that it does not involve name but can include anything relating to a person, such as height, weight, or demographic. The Committee noted that this is inconsistent with what is stated in the participant information sheet. The Committee noted that the information sheet states that the study sponsor will receive anonymised the data, thus implying that the data disclosed to the sponsor is identifiable. Please clarify this process in the information sheet.
2. Please note that HDECs do not support the stopping of trials for commercial reasons as noted in r.1.6.
3. Please remove all yes/no tickboxes from the consent form for choices that are not truly optional.
4. Please change the title ‘signatures page’ to ‘consent form’
5. Please simplify the privacy statement.
6. Please clarify on page 13 if the data transfer involves identifiable data.
7. Please localise the language in the information sheet and consent form.
8. Please add where tissue samples will be sent. Please provide which country and the laboratory if possible.
9. Please remove statements about needle-stick injuries form the information sheet.
10. Please remove the entire additional Clause 14 statement about additional research using data (pages 201-22), this is confusing and implies the release of identifiable data to the sponsor.
11. Please add a Māori tissue statement to the information sheet.
12. Please check all documents to ensure consistency on the fact that tissue samples will be identified.
13. Please amend the infant protection rights statements to be in line with those of other participants.
14. Please amend page nine of the information sheet to clearly state that there may be no benefit for trial participation.

Decision

This application was *provisionally approved* by consensus, 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* *para 6.22*).
* Please provide the outcome of SCOTT consultation.

This following information will be reviewed, and a final decision made on the application, by Dr Charis Brown and Ms Rosemary Abbott.

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| **5** | **Ethics ref:** | **16/NTA/180** |
|  | Title: | Blood biomarkers for detection of disease burden in patients with melanoma |
|  | Principal Investigator: | Prof. Cristin G Print |
|  | Sponsor: | The University of Auckland |
|  | Clock Start Date: | 03 November 2016 |

Professor Cristin Print and Dr Cherie Blankton 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 Karen Bartholomew and Dr Kate Parker declared potential conflicts of interest on this application.

The Committee decided that Dr Bartholomew could remain and participate in the decision.

The Committee decided that Dr Parker could remain but not participate in the discussion.

Summary of Study

1. The study aims to show that melanoma cancer relapse can be detected three to four months earlier by using genomic analysis on circulating cancer cells.

Summary of ethical issues (resolved)

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

1. The Committee queried how findings from the analysis would be relayed back to the participants’ GPs. The researchers explained that disclosure of findings that are relevant to a participant’s health will follow considerable discussion by the research team and any other relevant individuals.
2. The researchers noted that the study can be considered a pure observational research study but wondered if would be considered therapeutic due to the potential disclosure of incidental findings and requested any additional guidance on disclosure of incidental findings. The Committee stated that all disclosures of incidental findings should be done in line with the National Ethics Advisory Committee’s *Ethical Guidelines for Observational Studies* document.
3. The Committee queried the use of samples taken for treatment and if there the researchers would use these for their research if samples would be used up through use in the study. The researchers explained that if tissue samples would be destroyed by their use in this research study then those samples will not be used and the people who they belonged to would not be able to participate in the study. .
4. The Committee asked about the data linking process. The researchers stated that this will be done manually/
5. The researchers noted that they would be happy to set up a committee to determine the appropriateness of disclosing any incidental findings.
6. The Committee noted the high quality of the participant information sheet.

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

1. Please add Māori cultural support contact details to the participant information sheet.

Decision

This application was approved by consensus with the following non-standard conditions:

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

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| **6** | **Ethics ref:** | **16/NTA/181** |
|  | Title: | NIVORAD |
|  | Principal Investigator: | Mr Louis Lao |
|  | Sponsor: | NHMRC Clinical Trial Centre |
|  | Clock Start Date: | 03 November 2016 |

Dr Louis Lao and Dr Charlotte Cooper were present in person for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The study investigates using immunotherapy, in conjunction with radiotherapy, to increase survivability of stage four, non-small cell lung cancer. Currently immunotherapy has been shown to be superior to chemotherapy alone and the researchers believe that by combining the two therapies will increase survivability.

Summary of ethical issues (resolved)

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

1. The researchers stated that the radiation used in the study is very focused and precise and will not increase the participant’s chances of side effects from this.
2. The Committee queried the statement around participants paying for non-study medicines. The researchers explained that this statement is based on the Australian model and that the study drug, which can cost up to ten thousand dollars a month, will come free of charge.

Summary of ethical issues (outstanding)

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

1. The Committee stated that, in line with the HDEC Standard operating Procedures (SOPS)*,* the provision of material or financial support is not determinative of whether a study is conducted principally for the benefit for a manufacturer or distributor. The Committee recommend checking paras 145 to 145.5. of the SOPs to determine if this study counts as a sponsored trial or not. Please provide the outcome of this decision and update the ACC statement in the participant information sheet accordingly.
2. Please clarify if participants will receive the study drug for free as long as they respond to it or if the provision will cease on completion of the study. Please amend the participant information sheet to clearly state this.
3. Please provide procedures around the return of incidental findings that will be relevant to participant’s health and update the protocol accordingly.
4. Please provide an endpoint for the storage of samples for future unspecified use. Please include this in the participant information sheet. Indefinite storage is not supported by HDECs.
5. Please update the participant information sheets and consent forms so that there is a separate PISCF for future unspecified research and refer to the Future Unspecified Research guidelines and ensure the required information is included. The information in the paragraph on page 7 is not sufficient.
6. The Committee noted that lung cancer rates and mortality is very high for Maori, and requested that the researchers seek advice for ensuring recruitment is accessible to Maori (this may require more than open enrolment).

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

1. Add all cases of extra radiation exposure above those that can be expected as part of standard care.
2. Please update the risks section of the information sheet to separate the risks based on severity.
3. Pleasure insure that the consent form contains specific items to consent for access to previous medical records, previous sample and follow up to death (in lay language) and ensure these points are adequately covered in the PIS body.

Decision

This application was *provisionally approved* by consensus, 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* *para 6.22*).
* Please clarify how long the study drug will be provided for.
* Please provide separate information sheets and consent forms for future unspecified research
* Please advise the Committee about the determination of who, if any, can be considered the study sponsor. Please update the ACC statement in the information sheet accordingly.
* Please update the protocol to explain how incidental findings will be managed and disclosed. *(Ethical Guidelines for Intervention Studies* *Paras 5 – 5.11)*
* Please provide a duration of storage for the tissue used for future unspecified research and include this in the information sheet.

This following information will be reviewed, and a final decision made on the application, by Ms Rosemary Abbott and Dr Kate Parker.

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| **7** | **Ethics ref:** | **16/NTA/178** |
|  | Title: | Comparison of the blood levels of two forms of lorazepam 2.5 mg in healthy volunteers under fasting conditions |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Southern Cross Pharma Pty Ltd |
|  | Clock Start Date: | 03 November 2016 |

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

Potential conflicts of interest

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

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

Summary of Study

1. The study investigates the pharmacokinetics of two forms of lorazepam, a generic version and a market leader version.

Summary of ethical issues (resolved)

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

1. The Committee requested that all the side effects of the study drug be included in the participant information sheet.
2. The Committee was satisfied with the studies’ design and justification.

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

1. Please add a full list of side effects of lorazepam in the participant information sheet. Please categorize these by severity.

Decision

This application was *approved with non-standard conditions* by consensus. The non-standard conditions are:

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

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| **8** | **Ethics ref:** | **16/NTA/190** |
|  | Title: | Child and Famly Unit patient and whanau feedback. |
|  | Principal Investigator: | Dr Josephine Stanton |
|  | Sponsor: |  |
|  | Clock Start Date: | 03 November 2016 |

Dr Josephine Stanton 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 researchers want to understand what is of value in inpatient units. Areas such as autonomy, competence, and relatedness as examples of what aspects of care will be examined.

Summary of ethical issues (resolved)

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

1. The Committee queried the percentage of Māori involved in the study. The researcher explained that around 40% of their admissions are Māori and that 20% of inpatients are Māori.
2. The Committee asked about the outcome of Māori consultation. The researchers stated that they were instructed to add Māori contact details to the information sheet.
3. The Committee noted that the researcher and their management are involved in recruitment. The researcher explained that they and their manager will not be involved in recruitment and they themselves have done as much as possible to avoid them and their management from learning who is participating in the study.
4. The Committee asked if interviews will be one on one. The researcher explained that they will be conducted according to parental preference for under 16s and according to the preference of all participants over 16.
5. The Committee queried who will be performing the thematic analysis of the interviews. The researcher explained that they, their co-investigator, student, and cultural advisor will.
6. The Committee queried the qualifications of the student. The researcher explained that he has trained in interviewing and has previously worked with similar groups to the study population.

Summary of ethical issues (outstanding)

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

1. The Committee stated they had grave concerns over the potential for coercion in the study. The researcher explained that no one will be approached unless judged as able to consent by clinicians, further if their family does not agree to also participate then the inpatients will not be allowed to participate. The Committee reiterated that the risk of coercion remains high and that there need to be formalised procedures put in place to avoid this.
2. Please provide suitable information sheets and assent forms. This includes an information sheet and consent form for parents of participants unable to provide informed consent, an information sheet and consent form for participants able to provide their own informed consent (this includes all participants aged 16 years or older and may include some younger participants if they are deemed competent), an information sheet and assent form for children, and a very simple information sheet and assent form for young children that should very simply explain their participation in the study. Guidance on assent can be found at <http://ethics.health.govt.nz/guidance-materials/assent-guidance>.
3. The Committee noted that there needs to be a clear demarcation between assent and consent and for whānau and patients. Information for the parents needs to be about their participation and their child’s participation. These forms need to be separate. Please provide these documents.
4. Please confirm whether or not individuals treated under the Mental Health (Compulsory Assessment and Treatment) Act who are over the age of 16 are able to participate in research without conflicting with right 7.4 of the Code of Health and Disability Consumer’s rights. Research involving participants who are not competent to consent is inconsistent with the Bill of Rights unless it is undertaken in accordance with Right 7 (4) of the of the Code of Health and Disability Services Consumers’ Rights. In addition to requirements regarding ascertaining the views of the consumer and other suitable persons (forms consistent with this aspect are currently included in this application), Right 7(4) of the Code requires that any health services provided without the informed consent of the consumer must be in the best interests of the consumer. This means that there must be some benefit, or potential benefit, to the participant beyond what they would receive if they were not participating in the research.
5. Please provide what procedures are in place to ensure interviewer safety.
6. The Committee queried who will be performing the thematic analysis of the interviews. The researcher explained that they, their co-investigator, student, and cultural advisor will. Please explain how this will be done and if researchers will only analyse transcripts from individuals of their own culture.
7. The Committee asked how negative findings about the unit would be managed. Please include this in the study protocol.
8. Please provide detail in the protocol about how discussion of the study and consent for parents and consent for inpatients will be managed specifically when each group will be approached, what steps are included to determine consentability, and what mitigations to reduce harm are in place. If parents may be consented at a different time than inpatients will be consented/assented please explain this.
9. The Committee stated that you cannot collect the demographic, diagnosis, and DHB of origin of patients who have indicated that they do not want to participate in the study. These markers are considered identifiable health information. *The Ethical Guidelines for Observational Studies para 6.17* states that individuals have the right to withdraw from studies at any time and that this right must be explained and respected.
10. The Committee queried the suitability of bringing in an interviewer who had not been trained in Tikanga Māori and who spoke English as a second language. The researcher stated that the interviewer has experience of working in the setting and has excellent English. Additionally they have the unit’s cultural advisor available to be present for interviews for support. The Committee felt that having the unit’s cultural advisor be present would potentially add to the coercive nature of the study. Please address how this will be managed.
11. The Committee stated that the Mental Health (Compulsory Assessment and Treatment Act1992) prohibits the audio and visual recording of individuals under the act without that individual’s consent. Please make sure consent is explicitly sought for any audio or visual recording of participants who are under the act.
12. The Committee sought clarification on the study timeframes as they felt that the current timeline of 40 interviews in two months would cause the process to be rushed. Please confirm that this timeframe is correct and that this is feasible.

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

1. Please remove yes/no tickboxes from the consent form except for those statements that ticking no would exclude them from study participation.
2. Please make sure the language used in the participant information sheets are appropriate for the ages of the children involved.
3. Please include more information in the study protocol about what benefits, if any, come from study participation eg telling their own stories/being heard.
4. Please ensure participant rights are included eg right to have the recorded turned off if they are distressed or wish to stop, return of summary of results. Do they have the right to a transcript?

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 *(Ethical Guidelines for Observational Studies para 6.10)*
* Please provide suitable information sheets and assent forms. This includes an information sheet and consent form for parents of participants unable to provide informed consent, an information sheet and consent form for participants able to provide their own informed consent (this includes all participants aged 16 years or older and may include some younger participants if they are deemed competent), an information sheet and assent form for children, and a very simple information sheet and assent form for young children that should very simply explain their participation in the study. Guidance on assent can be found at <http://ethics.health.govt.nz/guidance-materials/assent-guidance>.
* Please confirm that participants who are under the Mental Health (Compulsory Assessment and Treatment) Act are legally able to provide informed consent to be in the study. The Committee stated that it is not possible for HDECs to approve an application unless it is consistent with New Zealand law, including the right not to be subjected to medical or scientific experimentation without that person's consent (section 10 of the New Zealand Bill of Rights Act 1990). Research involving participants who are not competent to consent is inconsistent with the Bill of Rights unless it is undertaken in accordance with Right 7 (4) of the of the Code of Health and Disability Services Consumers’ Rights. In addition to requirements regarding ascertaining the views of the consumer and other suitable persons (forms consistent with this aspect are currently included in this application), Right 7(4) of the Code requires that any health services provided without the informed consent of the consumer must be in the best interests of the consumer. This means that there must be some benefit, or potential benefit, to the participant beyond what they would receive if they were not participating in the research.
* Please address how the potential conflict of interest will be managed. *(Ethical Guidelines for Observational Studies paras 4.18-4.19)*
* Please provide the interviewer’s CV.
* Please provide the details of interviewer safety plans.
* Please provide evidence of how the thematic analysis will be performed and if advisors will only review the feedback of those of their own culture.
* Please provide justification for the follow up phone interview.
* Please address in the protocol how negative findings will be managed.
* Please amend the study documents to no longer collect demographic, DHB of origin, and diagnosis information. (*The Ethical Guidelines for Observational Studies para 6.17)*
* Please note health information is required to be kept for 10 years after the youngest participants turns 16.
* Please include information around, and specifically seek consent for, any audio or visual recordings that will be taken during the study

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

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| **9** | **Ethics ref:** | **16/NTA/184** |
|  | Title: | Are k-wires better to be buried or unburied |
|  | Principal Investigator: | Dr David Kieser |
|  | Sponsor: |  |
|  | Clock Start Date: | 03 November 2016 |

Dr David Kieser 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 is a randomised controlled trial that investigates any differences in outcomes in patients who have k-wires left standing proud from the skin or who have them buried.
2. The participants will mostly be children under the age of thirteen and will receive standard of care. Current standard of care leaves it to the surgeon’s discretion whether to leave the wires proud or under the skin.

Summary of ethical issues (resolved)

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

1. The Committee queried how potential participants will be identified. The researcher explained that they will note which children are going to the operating theatre for a k–wire operation and then approaching them pre-operatively but in a ward environment rather than in the Emergency Department.
2. The Committee enquired if patients with urgent conditions will have their care delayed so that the researchers can discuss the study with them. The researcher explained that they will not be approaching those patients who are urgent or who have received head injuries.
3. The Committee noted that the study is a pilot study and queried the two year follow up timeline. The researcher explained that there is a two year recruitment phase so they wanted to keep track of all participants as outcomes can be environment-dependent.
4. The Committee queried what the standard of care for k-wires is. The researcher explained that this is truly down to surgeon preference, with some surgeons changing from operation to operation. This study is therefore a randomised quality improvement audit (comparison of two standards of care).
5. The Committee asked how the researchers will determine GP costing. The researchers explained that the consent form gives participants the option to state if they have sought other medical care and the costs. The Committee stated that this can only be done with the expressly written consent of the participants.

Summary of ethical issues (outstanding)

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

1. The Committee noted that the Participant Information Sheet (PIS) is not acceptable in its current form. The PIS should be invitational, in lay language without medical jargon, explain clearly to parents the rationale for the research, what will happen to their child etc. The Committee strongly recommends that the researchers review the HDEC PIS template, but that the research writes the PIS as they would explain the study to a non-medical person. Please include the relevant letterheads etc. Please note that the risks listed are usual operational risks – this can be clearly stated, or if the risk profiles are different between the two procedures then explain this. Parents have the right to receive a summary of results. Please note that on the consent form parents should give specific consent for access to their child’s medical records (and the kind of information being collected).
2. The Committee noted that there are no assent forms for children. Please provide suitable assent forms. This includes an information sheet and consent form for parents of participants unable to provide informed consent, an information sheet and consent form for participants able to provide their own informed consent (this includes all participants aged 16 years or older and may include some younger participants if they are deemed competent), an information sheet and assent form for children, and a very simple information sheet and assent form for young children that should very simply explain their participation in the study. Guidance on assent can be found at <http://ethics.health.govt.nz/guidance-materials/assent-guidance>
3. The Committee requested the compensation wording is updated for accuracy, they suggested the following statement: *“If you were injured as a result of treatment given as part of this study, which is unlikely, you* ***won’t*** *be eligible for compensation from ACC. However, compensation would be available from the study’s sponsor, [x], in line with industry guidelines. We can give you a copy of these guidelines if you wish. You would be able to take action through the courts if you disagreed with the amount of compensation provided. If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.”*
4. The Committee noted the statistical commentary in b.2.2.1 and asked if the study is sufficiently powered. The researcher explained that there had been ongoing discussion about the primary outcome with the co-investigator. Please provide evidence that the study is sufficiently powered and at what level of outcome.
5. The Committee noted that the study protocol is minimal and does not fully explain the entire study process, evidence base, rationale, number of participants, measures, endpoints relating to the study and the validity of approaches to ensure costing data is accurate. Please ensure the study protocol fully explains all of these.
6. The Committee requested that the researchers retain data for 10 years from the time that under-16s turn 16.

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

1. Please clearly state in the information sheet that there may not be a definitive outcome of the study and that the study aims to evaluate the effectiveness of the two methods.

Decision

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

* Please ensure that all health information is stored for a minimum period of 10 years (Health (Retention of Health Information) Regulations 1996).
* Please amend the information sheet and consent forms, taking into account the suggestions made by the committee *(Ethical Guidelines for Observational Studies para 6.10)*
* The Committee were concerned the study was not sufficiently powered to show superiority. (*Ethical Guidelines for Intervention Studies* Appendix 1).
* Please ensure the study protocol covers the entire study process. *(Ethical Guidelines for Intervention Studies* *Paras 5 – 5.11)*
* Please provide suitable consent and assent forms for the study population. (*Ethical Guidelines for Intervention Studies* *para 6.22*).

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| **10** | **Ethics ref:** | **16/NTA/183** |
|  | Title: | Arthroresis screw in tibialis posterior reconstruction |
|  | Principal Investigator: | Dr David Kieser |
|  | Sponsor: |  |
|  | Clock Start Date: | 03 November 2016 |

Dr David Kieser 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 is a blinded trial of implanting an arthroresis screw in patients who are having foot reconstruction surgery. The standard medical rationale is that this splints the bone and helps it form deforming during the healing process.
2. The researchers wish to do this study as there is no literature on the outcomes of the use of the screw.
3. There is currently no standard of care for the use of Arthroresis screws, it is surgeon preference.
4. Participants in this study will be blinded as to whether or not they have had a screw implanted.

Summary of ethical issues (resolved)

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

1. The Committee queried what happens if the screw needs to be removed. The researchers explained that if needed the screw can be completely removed. The researcher noted that foot pain is a complex issue and that it is very rare that a single cause can be definitively attributed. A participant is likely to be unblinded in this case.
2. The Committee asked about the rationale for the study. The researcher explained that they support evidence based practice and wish to determine the best course of treatment.
3. The Committee asked about the necessity of the blinding and how the blinding would be ensured. The researchers explained that all patients, physios, radiographers will be blinded as the screw cannot be detected by hand. The researcher explained that patients will be more inclined to attribute any foot pain to the screw or the lack of the screw.
4. The Committee asked if patients would be public or private healthcare patients. The researcher explained that they would be recruiting from both.
5. The Committee was satisfied that a survey of foot and ankle surgeons about their preferred methods was low risk and could proceed through an Institutional Committee.

Summary of ethical issues (outstanding)

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

1. The Committee noted that recruitment numbers were reduced from 100 participants to 40 and asked if this was powered if unblinding occurred. The researchers explained that they would use data until withdrawal. Please provide evidence that the study is sufficiently powered if unblinding occurs.
2. The Committee stated that the current study protocol does not sufficiently detail the methods, rectuitment, selection, procedures, statistical justification, data requirements, data management of the study. Please amend the study protocol to include more detail, and review other study protocols as examples.
3. The Committee noted that the participant information sheet and consent forms did not follow the HDEC-recommended format. They suggested using the ones found at: [ethics.health.govt.nz](http://www.ethics.health.govt.nz).
4. Please re-write the PIS removing the medical jargon and writing in invitational lay language.
5. Explain randomisation in lay language to participants. Explain blinding (rationale, process, ability to request information and consequences of this). Participants have a right to the summary of their results. Include consent provisions for access to medical records. Document the standard of care and any additional risks and procedures related to the study (eg questionnaires, additional follow ups, additional X-rays) etc.
6. The Committee requested the compensation wording is updated for accuracy, they suggested the following statement: *“If you were injured in this study, which is unlikely, you would be eligible* ***to apply*** *for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery. If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.”*

Decision

This application was *provisionally approved* consensus, 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* *para 6.22*).
* Please ensure the study protocol fully explains the study methods. *(Ethical Guidelines for Intervention Studies* *Paras 5 – 5.11)*

This following information will be reviewed, and a final decision made on the application, by Dr Brian Fergus and Dr Kate Parker.

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| **11** | **Ethics ref:** | **16/NTA/192** |
|  | Title: | Comparison of the blood levels of two forms of phentermine 40 mg in healthy male and female volunteers under fed conditions |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Aspen Australia |
|  | Clock Start Date: | 03 November 2016 |

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

Potential conflicts of interest

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

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

Summary of Study

1. The study is a bioequivalence study investigating the blood levels of two forms of the drug Phentermine in participants. One of these formulations is a new medicine.
2. Participants will be given a 40 milligram test formulation or 40 milligrams of a market brand formulation.
3. Blood samples will be collected prior to dosing, and at specified times up to 72 hours of dosing.

Summary of ethical issues (resolved)

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

1. The Committee queried if this study is a feasibility study or a pilot study. The researchers explained that it is a pilot study and that it is extremely difficult to determine the blood metabolism of the drug. The outcomes of this study will determine if any further amounts of the study drug are produced as it is very expensive.
2. The Committee stated that pilot studies do not evaluate drug effectiveness. The Researchers stated that the aim of this study is simply to determine the blood profile of the drug, and not the effectiveness. Results from this study will help shape the development of any future research on the study drug.
3. The Committee queried the photo identification of participants and video cameras in the units. The researcher explained that the photos are for the purposes of verifying the identity of the participants. The video cameras are required by the sponsor in order to show that there are participants in the trial. Photographs will later be destroyed.
4. The Committee asked where blood samples will be going for testing. The researchers explained that the lab is on-site.

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

1. Add area codes for all phone numbers.

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 *(Ethical Guidelines for Observational Studies para 6.10)*

This following information will be reviewed, and a final decision made on the application, by Dr Christine Crooks and .Ms Rosemary Abbott.

## 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:** | 06 December 2016, 01:00 PM |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

The following members tendered apologies for this meeting.

1. **Problem with Last Minutes**

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

The meeting closed at 6:05pm.