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| **Committee:** | Northern B Health and Disability Ethics Committee |
| **Meeting date:** | 21 November 2012 |
| **Meeting venue:** | Novotel Tainui, 7 Alma Street, Hamilton |

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| **Time** | **Item of business** |
| 12:00pm | Welcome |
| 12.10pm | Confirmation of minutes of meeting of 24 October 2012 |
|  | New applications (see over for details) |
| 12:30 – 1:00 | i 12/NTB/55 (Stephanie/Mali) |
| 1:00 – 1:30 | ii 12/NTB/56 (Paul/Mary-Anne) |
| 1:30 – 2:00 | iii 12/NTB/57 (Kerin/Paul) |
| 2:00 – 2:40 | iv 12/NTB/58 (Mary-Anne/Kate) |
| 2:40 – 3:20 | v 12/NTB/59 |
| 3:20 – 3:50 | vi 12/NTB/60 |
|  | General business:  Noting section of agenda |
| 4:25pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Mrs Raewyn Sporle | Lay (the law) | 01/07/2012 | 01/07/2015 | Present |
| Mrs Maliaga Erick | Lay (consumer/community perspectives) | 01/07/2012 | 01/07/2014 | Present |
| Mrs Mary Anne Gill | Lay (consumer/community perspectives) | 01/07/2012 | 01/07/2015 | Present |
| Mrs Kate O'Connor | Non-lay (other) | 01/07/2012 | 01/07/2015 | Present |
| Mrs Stephanie Pollard | Non-lay (intervention studies) | 01/07/2012 | 01/07/2015 | Present |
| Dr David Stephens | Lay (consumer/community perspectives) | 01/07/2012 | 01/07/2014 | Present |
| Dr Paul Tanser | Non-lay (health/disability service provision) | 01/07/2012 | 01/07/2014 | Present |
| Ms Kerin Thompson | Non-lay (intervention studies) | 01/07/2012 | 01/07/2015 | Present |

## Welcome

The Chair opened the meeting at 12:00pm and welcomed Committee members.

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 24 October 2012 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **12/NTB/55** |
|  | Title: | LATITUDE |
|  | Principal Investigator: | Dr Frank Kueppers |
|  | Sponsor: | Janssen-Cilag (New Zealand) Limited |
|  | Clock Start Date: | 09 November 2012 |

Dr Frank Kueppers was not available 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 ethical issues

The main ethical issues considered by the Committee were as follows.

* The Committee notes no major ethical concerns with the study.
* Please supply evidence of independent scientific peer review for the study.
* Please clarify if SCOTT approval is pending or has been obtained.
* Please clarify and detail provisions for a DSM committee (r.1.5). For example, has the committee been commissioned and what is its constitution?
* Please clarify if tissue samples will be stored and used for future research? There is inconsistent information in the application form (b.4.5) and the patient information sheet and consent forms.
* The Committee is not satisfied that there are no cultural issues as stated (p.4.2). Clearly there are cultural issues relating to the use of tissue for Maori. Please clarify and detail how cultural issues pertaining to tissue samples (e.g. the use and disposal) will be addressed.
* Please clarify and detail the provisions to address safety issues regarding the cardiotoxicity of the drug used in the study. The Committee notes that an ECG is done as part of pre-study screening. However, it is expected that echocardiograms would be performed during screening as well as for ongoing monitoring throughout the study.
* Please clarify and provide details on how confidentiality will be ensured (r.2.3). For example what the "appropriate measures" are.
* The Committee requested the following changes be made to the Participant Information Sheet:
  + please condense and remove duplicated information. Twenty-seven pages is too long,
  + please provide a simplified title – it is too technical as it stands,
  + please remove the reference to U.S. Law (page 1),
  + please clarify the availability of the drug in New Zealand (page 2),
  + please rephrase “flipping a coin” – research indicates that cancer patients do not like this wording used to describe randomisation,
  + the table is not ‘below’ (page 5) but on the following page. Please amend,
  + please remove the asterisks from the comments (page 6),
  + please explain, in lay language, the abbreviations used in the table,
  + is the fourth bullet on page eight useful for the participant? Consider removing or clarifying,
  + please clarify what samples will be taken, for what purpose and where they will be sent overseas. For example, the biomarker study is not done in New Zealand but yet it is in the PIS (page 7-8),
  + please insert the word ‘if’ before ‘abiraterone acetate’ as the sentence implies the study drug will be effective (page 10),
  + please clarify whether the disposal of tissue sample overseas satisfies Maori cultural issues (page 20-21),
  + please ensure that the document is written in New Zealand (British) English,
  + please ensure that all relevant information is updated in their respective [brackets] (e.g. page 8, 9, 18),
  + please note that participants’ GP has to be notified, it is not an option. Please amend accordingly (page 25),
  + please note that agreeing to an auditor (page 25) is not an option; participants have to agree to it. Please leave the clause in but remove the tick box,
  + please make the boxes bigger for the participants to insert their initials,
  + please include Maori health support contact details.

Decision

This application was *provisionally approved* by consensus, subject to the above amendments being addressed, and a resubmission of the revised versions of the PIS and CF.

This following information will be reviewed, and a final decision made on the application, by the Chair, Mrs Stephanie Pollard and Mrs Maliaga Erick.

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| **2** | **Ethics ref:** | **12/NTB/56** |
|  | Title: | Probenecid boosting of flucloxacillin |
|  | Principal Investigator: | Dr Richard Everts |
|  | Sponsor: | Nelson Marlborough District Health Board |
|  | Clock Start Date: | 07 November 2012 |

Dr Richard Everts 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 ethical issues

The main ethical issues considered by the Committee were as follows.

* The Committee notes that this is a worthwhile study that has huge potential benefits to both patients and the medical sector.
* The Committee notes that there are no major scientific validity issues.
* The Committee commends the research team for putting together the PIS which is easy to read and in plain English.
* The Committee requested the following changes be made to the Participant Information

Sheet:

* + the inserts are difficult to read. Please consider enlarging or removing unnecessary information,
  + page 1 states that “these patients have almost all been cured”. Please reword the sentence using more neutral language,
  + page 2 (para 1) states “we will test each volunteer’s blood and by a more modern technique”. Please clarify what specific tests will be done (e.g. serum creatinine and creatinine clearance),
  + the ACC compensation wording is not sufficient. The Committee recommends using the standard ACC compensation text,
  + please include Maori health support contact details,
  + please refer to the correct ethics committee, the Northern B Health and Disability Ethics Committee, in all instances.
* The Committee requested the following changes be made to the Consent Form:
  + please include a request for interpreter at the beginning of the consent form,
  + please refer to the correct ethics committee, the Northern B Health and Disability Ethics Committee, in all instances.

Decision

This application was *approved* by consensus with administrators to review the comments.

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| **3** | **Ethics ref:** | **12/NTB/57** |
|  | Title: | 0.9% Saline vs. Plasma Lyte® 148 for Fluid Resuscitation in Intensive |
|  | Principal Investigator: | Dr Paul Young |
|  | Sponsor: | Medical Research Institute of New Zealand |
|  | Clock Start Date: | 07 November 2012 |

Dr Paul 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 ethical issues

The main ethical issues considered by the Committee were as follows.

* The Committee notes no major ethical concerns with the study.
* The Committee discussed the following issues with the researcher and was satisfied with the answers provided.
  + The primary and secondary endpoints the research team will be measuring and whether they have sufficient statistical power. Participant numbers are based on a similar study and allows for attrition and conservative recruitment rates.
  + Who is providing statistical advice and analysis? Statistical advice and analyses will be performed by the Intensive Care Unit team at Monash University, which includes a Professor in Statistical Research.
  + please clarify if patients will receive a copy of the signed PIS/CF. The researcher confirmed that all potential participants will receive a copy of the PIS and only those who opt out of the study will sign the opt-out form.
* The Committee requested the following changes be made to the Participant Information Sheet:
* page 2 “it is not clear which fluid is the best one to use”. Please elaborate on the purpose of using a fluid
* please refer to the correct ethics committee, the Northern B Health and Disability Ethics Committee, in all instances

Decision

This application was *provisionally approved* by consensus, subject to the above amendments being addressed, and a resubmission of the revised versions of the PIS and CF.

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

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| **4** | **Ethics ref:** | **12/NTB/58** |
|  | Title: | Use of Keragel to treat lesions in the mouth |
|  | Principal Investigator: | Dr Clive Marsh |
|  | Sponsor: | Keraplast |
|  | Clock Start Date: | 09 November 2012 |

Dr Clive Marsh and Sharon Cassidy 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 ethical issues

The main ethical issues considered by the Committee were as follows.

* The Committee is concerned that there are significant ethical issues with the study.
* The Committee is concerned that there are no references provided with regard to the safe use of Keragel in the mouth; safety has only been established for skin lesions.
* The Committee questions whether Keragel needs to undergo SCOTT review given that it will be applied in the mouth and subsequently ingested.
* The Committee was informed that the potential participants for this study would be a very specific group of patients with a rare condition (that results in blisters on the skin). Therefore, not anyone with lesions in their mouth will be eligible for the study but only patients with the rare condition who present with lesions in their mouth as well. This has to be made clear.
* The Committee is extremely concerned about the proposed sample size of five participants. The Committee feels this is not a sufficient number to establish any significant findings even for a pilot study. The Committee is concerned that no statistical advice has been obtained.
* The Committee is also extremely concerned that no scientific peer review has been obtained (b.2.2.1) and that the reason given is that “the study is low risk”. Not only is this an unsatisfactory answer, but furthermore on page 3 of the application form, the researchers admit that the ‘agent’ carries a medium to high risk (a.2.1.3). The Committee is extremely unsatisfied with the scientific rigor of the proposed study.
* The Committee would like some assurance that the insurance indemnity amount of NZD$250000 is sufficient as it seems relatively lower than other studies.
* However, the Committee also notes that Epidermolysis bullosa is a terrible inherited disease for which there is currently no therapy other than palliative moisturising ointments and surgery and commends the research team’s intentions.
* As such, the Committee would like to offer some helpful recommendations which the research team may want to consider should they so wish.
  + Conduct a pilot study in animals in the first instance.
  + If there is no toxicity in animals, a placebo controlled toxicity study could be done in normal volunteers.
  + If the above show some measureable benefit and no serious toxicity, perhaps a double blind randomised oral study in human participants could be conducted.
* The Committee requested the following changes be made to the Participant Information Sheet:
* please improve the readability,
* please reword “disrupt your digestive system” to “you may experience some indigestion”,
* a separate PIS/CF is required for the caregivers of participants younger than 16 years old,
* please include more information regarding application of the gel. For example, who will be applying the gel, will it only be applied in a clinical setting, will participants be able to apply the gel at their discretion.
* The Committee requested the following changes be made to the Consent Form:
  + add text for requesting interpreters using the standard format available on the HDEC website
  + “the study designed to assess burn healing and scar minimisation with keratin based dressings”. Please remove as it relates to another study.

Decision

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

These ethical standards are contained in the *Ethical Guidelines for Intervention Studies.* The references in the table below are to paragraph numbers in this document.

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| **Reference** | **Reason for declining** |
| **3.11** | The potential risks of an intervention study must be proportional to the potential benefits. |
| **5.5** | Scientific soundness is ethically important. Projects without scientific merit needlessly expose participants to risk and misuse their time, and waste resources. |
| **5.6** | The intended number of participants in an intervention study should be sufficient to generate reliable study findings, and the consequent recruitment targets should be realistic. Statistical issues relating to trial design, sample size and analysis can be complex, and usually require expert advice. |
| **5.11** | Peer review of the scientific validity of a study’s protocols is beneficial, and is advised for all studies that pose more than minimal risk. |
| **6.1** | Adequate recruitment is important to ensure that the number of participants is sufficient to reliably answer the study question(s). |

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| **5** | **Ethics ref:** | **12/NTB/59** |
|  | Title: | The molecular basis of Autism Spectrum Disorder (ASD) and other neurod |
|  | Principal Investigator: | Professor Russell Snell |
|  | Sponsor: | The University of Auckland |
|  | Clock Start Date: | 09 November 2012 |

Professor Russell Snell and Dr Jessie Jacobsen 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 ethical issues

The main ethical issues considered by the Committee were as follows.

* The Committee notes this is a very positive and worthwhile study.
* The Committee would like to congratulate Dr Jessie Jacobsen on being awarded the prestigious Rutherford Discovery Fellowship.
* The Committee discussed the following issues with the researcher and was satisfied with the answers provided.
  + Provisions for getting more funding; what if funding runs out part-way through the study? The researchers informed the Committee that more funding has been secured from the Rutherford Discovery Fellowship and the Oakley Foundation. Fundraising provisions have also been made and will be progressed once ethical approval has been granted.
  + “Determining participation based on criteria” as described in the protocol. The researchers informed the Committee that the criteria is a “moving feast” and will evolve as the study progresses and more information regarding the type and numbers of genes involved becomes more apparent.
  + The inclusion and exclusion described in f.2.1. The researchers reassured the Committee that only participants that have been clinically diagnosed with Autism Spectrum Disorder or other neurodevelopmental disorders will be included in the study.
  + Are there any provisions in place to reconsent a participant when he/she reaches the age of 16 years? The researchers informed the Committee that contact will be made when a participants turns 16 years old and reconsent obtained; the participant may choose to withdraw from the study if they so wish.
  + Who will be performing the metabolic and microbiology tests? These tests will be performed by Dr Mike Taylor at the University of Auckland, School of Biological Sciences.
  + Who is providing statistical advice and performing statistical analyses? The researchers informed the Committee that statistical advice and analyses will be provided by:
    - Professor Jim Gusella and Dr Michael Talkowski of Massachusetts General Hospital, Hardvard Medical School and the Broad Institute. Professor Gusella and Dr Talkowski have developed innovated high-throughput DNA sequencing strategies and bioinformatic analysis platforms for the resolution of molecular changes in complex neurodevelopment disorders.
    - Dr Klaus Lehnert, Honorary Associate Professor at The University of Auckland. is a bioinformatics specialist and has spent 11 years working in genetics and bioinformatics for ViaLactia Biosciences (NZ)Ltd.
    - Associate Professor Cristin Print and Associate Professor James Curran of The New Zealand Bioinformatics Institute. The bioinformatics Institute provides services for NZGL customers using sequence generated at the Center for Genomic and Proteomics (CGP).
* The researchers clarified that the option for tissue samples to be returned will be made available (question r.3.11.)
* The researchers clarified that the study will contribute to reducing inequities in health outcomes between different populations (f.1.1.)
* The Committee requested the following changes be made to the Participant Information Sheet:
* a separate patient information sheet and consent form for children.

Decision

This application was *approved* by consensus with administrators to review the comments.

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| **6** | **Ethics ref:** | **12/NTB/60** |
|  | Title: | The Odyssey trial |
|  | Principal Investigator: | Dr Ralph Stewart |
|  | Sponsor: | Covance Pty Ltd. |
|  | Clock Start Date: | 09 November 2012 |

Dr Ralph Stewart, Mr Chris McConachy (Covance) and Ms Sarah Douglas 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 ethical issues

The main ethical issues considered by the Committee were as follows.

* The Committee was reassured that every effort will be made to ensure there is a representative sample of Maori participants in the study given the higher burden of CVD in the Maori population.
* The Committee was concerned that for the purposes of blinding, participant LDL-C levels will not be disclosed throughout the duration of the study which is five years. The Committee feels that some provision has to be in place for the information to be released if necessary.
  + The researchers reassured the Committee that although LDL-C information will not be released to the participants, it will be closely monitored. Should the participant’s LDL-C levels fall below the stated threshold, there is an unblinding process in place.
  + The researchers reassured the Committee that although there is no “upper” threshold, the potential participants will already be on medication for their LDL-C levels, which tend to stay constant over time unlike other chronic conditions such as high blood pressure.
* Please clarify which ACC equivalents are not available and why (r.1.9.); the health and disability ethics committee’s standard operating procedures (SOPs) require that at the very least, ACC-equivalent compensation is available (page 33, para 148, 149). Please supply the exact compensation provisions for the study.
* The Committee was reassured by the researchers that emergency contacts supplied to the participants will be available 24 hours a day via a local New Zealand phone number. The emergency contacts will also know how to unblind participants if necessary.
* P4.1. States that people who participate in trials have a better health outcome. The Committee would like to suggest the research team be cautious in using this argument given the Cochrane meta-analysis published data.
* The letter to GPs should specify that specific monitoring procedures have been put in place to just monitor low LDL-C levels and not high LDL-Cs as well.
* The Committee requested the following changes be made to the Participant Information Sheet:
* please update all [TBC] instances as appropriate,
* please remove the sentence “We expect this will take about [TBC] minutes” as no time expectation is required,
* please remove the reference to U.S. Law (page 2),
* “which will be done 8 weeks after the end of study if you are still receiving the study drug when the study ends”. Please include and clarify that all participants will be contacted and a post-assessment carried out and not just participants receiving the drug,
* please make it clear that tissue samples will be sent overseas and maintained for future use in a tissue bank,
* please include Maori health support contact details for the various sites,
* please confirm and use an informative lay title (other than “The Odyssey Trial”).

Decision

This application was *provisionally approved* by consensus, subject to the above amendments being addressed, and a resubmission of the revised versions of the PIS and CF.

This following information will be reviewed, and a final decision made on the application, by the Chair, Mrs Kate O’Connor and Ms Kerin Thompson.

## 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:** | 19 December 2012 |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Auckland |

The meeting closed at 4:25pm.