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| **Committee:** | Southern Health and Disability Ethics Committee |
| **Meeting date:** | 14 October 2014 |
| **Meeting venue:** | Sudima Hotel, Christchurch Airport, 550 Memorial Avenue, Christchurch |

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| **Time** | **Item of business** |
| 12.00pm | Welcome |
| 12.05pm | Confirmation of minutes of meeting of 16 September 2014 |
|  | New applications (see over for details) |
| 12.30pm  4.00pm | i 14/STH/145  ii 14/STH/148  iii 14/STH/149  iv 14/STH/150  v 14/STH/152  vi 14/STH/155  vii 14/STH/156 |
| 4.05pm | General business:   * Noting section of agenda |
| 4.15pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Ms Raewyn Idoine | Lay (consumer/community perspectives) | 01/07/2012 | 01/07/2015 | Present |
| Mrs Angelika Frank-Alexander | Lay (consumer/community perspectives) | 01/07/2012 | 01/07/2015 | Present |
| Dr Sarah Gunningham | Non-lay (intervention studies) | 01/07/2012 | 01/07/2015 | Present |
| Dr Nicola Swain | Non-lay (observational studies) | 01/07/2012 | 01/07/2015 | Present |
| Dr Mathew Zacharias | Non-lay (health/disability service provision) | 01/07/2012 | 01/07/2015 | Present |
| Dr Devonie Waaka | Non-lay (intervention studies) | 01/07/2013 | 01/07/2016 | Present |
| Assc Prof Mira Harrison-Woolrych | Non-lay (intervention studies) | 01/09/2014 | 01/09/2015 | Present |
| Dr Fiona McCrimmon | Lay (the law) | 01/09/2014 | 01/09/2015 | Present |

## Welcome

The Chair opened the meeting at 12.20pm 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 16 September 2014 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **14/STH/145** |
|  | Title: | Efficacy and Safety Study of RPC1063 in Relapsing Multiple Sclerosis |
|  | Principal Investigator: | Dr Deborah Mason |
|  | Sponsor: | PPD Australia Pty Ltd |
|  | Clock Start Date: | 02 October 2014 |

Dr Deborah Mason was not present for discussion of this application.

Potential conflicts of interest

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

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

Summary of ethical issues

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

* The study is a multicentre, randomized, double-blind, double dummy, active controlled, parallel group study of oral RPC1063 in adult patients with relapsing multiple sclerosis..
* The study drug is not licenced in New Zealand. The participants will be randomly assigned 1:1:1 to receive RPC1063 0.5 mg once daily, RPC1063 1 mg once daily, or IFN β1a 30 μg intramuscular (IM) weekly for a period of at least 12 months. Patients will continue to receive randomized, blinded treatment until the last patient randomized has been treated for 12 months.
* The Committee noted that A.1.6 stated there were no ethical concerns for the study. However the Committee identified the following ethical concerns: i) this is an experimental drug that may have no benefit for the participant, ii) the drug may worsen their health (for example by causing adverse reactions as listed in the PIS) and iii) potentially poses a risk to any potential foetus.
* The Committee added that the CHMP Scientific Advice document (which was accepted as evidence of peer review of the study) discussed some risks of the experimental drug (e.g. bradycardia) which would have been appropriate to add in the relevant section of the application.
* The Committee noted that the risks were covered in the supporting documentation (e.g. the PIS, GP letter) but should be in the appropriate section of the application too.
* The application should also detail how the risks identified will be managed during the study.
* The Committee queried how the risk of the drug interactions would be managed by the researcher.
* The committee noted that the applicant had not provided a summary of the possible benefits of RPC 1063 in patients with relapsing MS in the relevant section of the application form.
* The Committee stated that the patient information sheet was very long and may therefore hide important information. For example, participants can’t drive after the first study dose, please ensure this is made clear before participants attend the first appointment.
* The Committee considered the generic sponsor statements, such as ‘all medicines have risks’, are not relevant and should be more specific in relation to this study and this study drug.
* The Committee commended the lay study title.
* The Committee stated that the PIS/CF was well formatted.
* The Committee queried whether the comparator drug was the best standard of care in New Zealand? Please clarify what the best standard of care is in New Zealand, and make this explicit for participants if it is not and justify the use of this comparative treatment arm.
* Please explain whether it is possible for patients to stay on the experimental drug after the end of the study? Justify this.
* Please clarify how this study meets equipoise.
* The Committee requested the following changes to the Participant Information Sheet and Consent Form:
* On pg.10 please include a subtitle heading for the Maori section.
* Please include a lay language explanation on page 11 for ‘nasal pharyngitis’.
* Please amend the statements about the drugs being approved in late 2014. These have now been approved.

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*).
* An intervention study meets the best intervention standard if the intervention(s) in the study are tested against the best proven intervention(s) available outside the study. In many settings there might be more than one intervention that is equivalent to the best, according to the current evidence. Please explain whether the comparative arm is the standard practice in New Zealand (*Ethical Guidelines for Intervention Studies* *para 5.13*).

This following information will be reviewed, and a final decision made on the application, by Ms Raewyn Idoine and Dr Sarah Gunningham.

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| **2** | **Ethics ref:** | **14/STH/148** |
|  | Title: | BO28984: A randomized, phase III study comparing alectinib versus crizotinib in treatment-naïve ALK-positive advanced non-small cell lung cancer |
|  | Principal Investigator: | Associate Professor Mark McKeage |
|  | Sponsor: | The University of Auckland |
|  | Clock Start Date: | 02 October 2014 |

Associate Professor Mark McKeage was not present for discussion of this application.

Potential conflicts of interest

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

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

Summary of ethical issues

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

* This is a randomised, active controlled, multicentre, phase III, openlabel study to evaluate and compare the efficacy of alectinib versus crizotinib in patients with treatment naive ALK positive advanced non-small cell lung cancer.
* This study will recruit 6 participants in New Zealand with a total of 286 participants worldwide.
* The Committee noted that the median survival was 12 months once diagnosed.
* The Committee noted that the experimental study drug, as well as the control arm treatment, is not available in New Zealand.
* The Committee noted a SCOTT application has been submitted.
* The Committee noted that an independent data safety monitoring committee is established.
* Please explain how the study meets equipoise, as this question is not correctly answered in application. The Committee understands the study is randomised between the arms, but please explain how there is genuine uncertainty between the two drugs. What evidence justifies equipoise standard?
* The Committee requested the following changes to the Participant Information Sheet and Consent Form:
* Pg.6 please reword “You will be asked to take alectinib or crizotinib until your disease gets worse”.
* Please remove information about having to pay for medicine and clinic visits, this is not relevant for New Zealand participants “After your participation in the study ends, you will need to pay for medicines and clinic, hospital, and doctors’ services that are part of your regular medical care”.
* Please seek advice on what information should be included for Maori participants in relation to use of human tissue and amend PIS/CF. Please view page 15 of Te Ara Tika: Guidelines for Māori research ethics: A framework for researchers and committee members. This is accessible from the HRC website.
* Please include a lay study title.
* On some pages the text merges into footer – please review formatting.
* Please be consistent with side effects formatting – one is a list one is a paragraph.

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*).
* An intervention study meets the equipoise standard if the evidence is ‘equally poised’ as to the overall balance of risks and benefits of each of the interventions offered in the study, so that it cannot be determined in advance which of the groups in a proposed study will be better off. Please explain how your study meets this standard. (*Ethical Guidelines for Intervention Studies* *para 5.18*).

The above information will be reviewed, and a final decision made on the application, by Secretariat.

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| **3** | **Ethics ref:** | **14/STH/149** |
|  | Title: | CLDK378A2205 |
|  | Principal Investigator: | Associate Professor Mark McKeage |
|  | Sponsor: | The University of Auckland |
|  | Clock Start Date: | 02 October 2014 |

Associate Professor Mark McKeage was not present for discussion of this application.

Potential conflicts of interest

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

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

Summary of ethical issues

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

* The Committee noted that the study will only involve 6 patients in New Zealand.
* The Committee stated that in the application form there was insufficient information about the risks involved in study participation but noted that this was elsewhere in the supporting documents. Please include more detail in the appropriate section of the application form in future applications.
* Information on contraception in the PIS is of low quality and poorly expressed. Please seek expert advice and revise this section, providing relevant and accurate information on contraception which may be used during this study
* Remove the interpreter statement if this is not available for participants.
* The Committee stated that this study should have an independent data safety monitoring committee – please clarify what safety monitoring is in place.
* The Committee requested the following changes to the Participant Information Sheet and Consent Form:
* Please include a lay title.
* Please move contact information to the front of the document.
* Please put a clear header - ‘Side Effects of Study drug’ as sub-heading for pg.12 information on possible adverse effects of study drug.
* Please put serious risks relating to the study medication at the start of risk section of PIS, not blood samples (risks related to blood sampling may be moved down).
* Please include incident rates for risks where possible.
* Please bold the serious risks – such as developing shortness of breath.
* The biomarker patient information sheet needs more detail. Please view the Ministry of Health guidelines 2007 for future unspecified research, it covers information to include, for example please include where tissue is stored, for how long, cultural issues, consistent font.

Decision

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

* Provide details of the Data Safety Monitoring *(Ethical Guidelines for Intervention Studies para 6.50).*
* Please amend the information sheet and consent form, taking into account the above 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 Ms Raewyn Idoine.

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| **4** | **Ethics ref:** | **14/STH/150** |
|  | Title: | Ipratropium bromide bioavailability study administered with and without concurrent oral charcoal |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Cipla Limited |
|  | Clock Start Date: | 02 October 2014 |

Dr Noelyn Hung, Dr Tak Hung and Ms 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 ethical issues

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

* The researchers explained the study, stating that it was a pilot study to test new kind of bioequivalence. The researchers explained that this was a pilot study assessing the pharmacokinetics of oral ipratropium bromide with and without concomitant oral charcoal ingestion
* The Committee explained that the study aims to study bioavailability rather than bioequivalence.
* Committee queried why there is screening for HIV and syphilis. The researchers explained that the sponsor has requested this, as staff will handle blood vials.
* Researchers confirmed they would inform participants of any incidental findings discovered during screening tests.
* The Researchers confirmed participants are referred to a website for study results. This is on the ICF.
* The Researchers confirmed that each person is individually consented.
* The Researchers confirmed they planned to run all study procedures on the same day, for all participations, with the same washout period for everyone.
* The Committee requested the following changes to the Participant Information Sheet and Consent Form:
* There is no need to state ‘this won’t affect the care you receive’ as these are healthy volunteers.
* Please review exclusion criteria, as #3 reason is a double negative and #11 may be incorrect.

Decision

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

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| **5** | **Ethics ref:** | **14/STH/152** |
|  | Title: | Echocardiographic Review of Dynamic Diastolic Function and Preload Markers in Age Matched Normal Population and Fontan Patients. |
|  | Principal Investigator: | Doctor Kathryn Rice |
|  | Sponsor: |  |
|  | Clock Start Date: | 02 October 2014 |

Doctor Kathryn Rice 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.

* Dr Rice explained that the study will recruit children who have had a Fontan operation, which results in only one heart chamber working instead of two. This results in shorter life expectancy and circulation problems.
* Dr Rice added there has been a lot of research into the circulation of Fontan patients however there were knowledge gaps. Up until now it has been difficult to observe what happens with circulation during exercise. This has changed in the last few years as echocardiographic imaging makes it feasible to observe.
* This is a novel use of this technology for this participation group. This study is a feasibility study to see if there is a way to establish the difference between regular heart controls verses participants who have the Fontan surgery.
* Initial feasibility is only occurring in New Zealand. There will be 15 normal controls and 15 Fontan participants.
* The Committee queried how the healthy population group would be recruited? Dr Rice explained that they are looking at 11 year olds up to adulthood. The plan is to age match participants from the Fontan group to the normal controls. This will be done by sending information to high schools and universities, around the hospitals including outpatient clinics.
* The Committee suggested approaching siblings of Fontan participants as a potential for age matches. Dr Rice confirmed this was an option and they did plan to talk to outpatients about this as a possibility. The Committee stated it would be easier to ask the Fontan patients if they had any friends of similar age as another option. Dr Rice explained the difficulty with this was because they were flying Fontan patients around the country it would be difficult to involve the participant’s friends.
* The Committee queried if there is a Fontan register. Dr Rice confirmed there was an Australasian registry with 1000 recruited. New Zealand has 25% of the Fontan population.
* Dr Rice explained that the Fontan participants will have screening and testing to ensure the exercise component is appropriate and there are no significant risks. If they were not able to safety participate they would be precluded from the study.
* The Committee queried if there is an internal safety monitor to ensure safety during the exercise testing. Dr Rice confirmed all vital signs would be monitored during the exercise period.
* The Committee queried if there is a formal review of data for safety monitoring. Dr Rice explained that if an acute event occurred they have the means to resuscitate and will review process internally, patient by patient.
* The Committee noted that the PIS was not age appropriate for younger participants.
* Please make it clear who gets the 60 dollars (the child or the parent?). Make it clear that it is reimbursement for travel and time expenses. Also make it clear that there is only one payment, even if parent and child are involved.
* Please note that health data derived from the study must be stored for a minimum of 10 years according to the [Health (Retention of Health Information) Regulations 1996](http://legislation.govt.nz/regulation/public/1996/0343/latest/DLM225650.html). For children under 16 years old, information must be stored until the last child turns 10 years from the youngest child turning 16.
* Please remove the word ‘folk’. Replace with ‘people’.
* The Committee noted that some children under 16 may be able to provide consent. Please explain how you plan to manage how some may be able to consent.
* The researcher explained the children have the opportunity to countersign the parent PIS/CF.
* The Committee noted that some children may be able to consent themselves, with parents providing assent. This required additional PIS/CF to be created for the study.
* The committee stated that if they do not assent to research then the participants should not be coerced to participate.
* The committee queried if Fontan participants are equivalent in intellectual ability compared to the healthy controls. The researcher explained there is a range. The surgery can result in learning difficulties – but only consenting participants are involved.
* The Committee requested the following changes to the Participant Information Sheet and Consent Form:
* The Committee noted that the study required a patient information sheet that was age appropriate (11 – 15 year olds) in order to facilitate assent, as well as a 15-17 year old patient information sheet for children who were competent enough to consent for themselves.
* Please review ‘you your’ to ‘their / the patient’. Make consistent and personal.
* Please remove ‘waiting to start the study and are awaiting approval’.
* Please make it clear that food and drink will be provided at no cost.
* For the control PIS please make it clear from the beginning that this is for healthy controls – currently may cause undue stress as it does not state why the child has been approached to participate.

Decision

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

* Please amend the information sheet and consent form, and assent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Observation Studies* *para 6.11*).
* Please provide an assent form for non-consenting participants to sign (*Ethical Guidelines for Observation Studies 6.21)*

This following information will be reviewed, and a final decision made on the application, by Ms Raewyn Idoine and Dr Sarah Gunningham.

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| **6** | **Ethics ref:** | **14/STH/155** |
|  | Title: | Study to evaluate the efficacy of IPI-145 administered in combination with rituximab vs placebo in combination with rituximab in subjects with previously treated CD20 positive Follicular Lymphoma. |
|  | Principal Investigator: | Dr Peter Ganly |
|  | Sponsor: | Infinity Pharmaceuticals, Inc |
|  | Clock Start Date: | 02 October 2014 |

Dr Peter Ganly was not present for discussion of this application.

Potential conflicts of interest

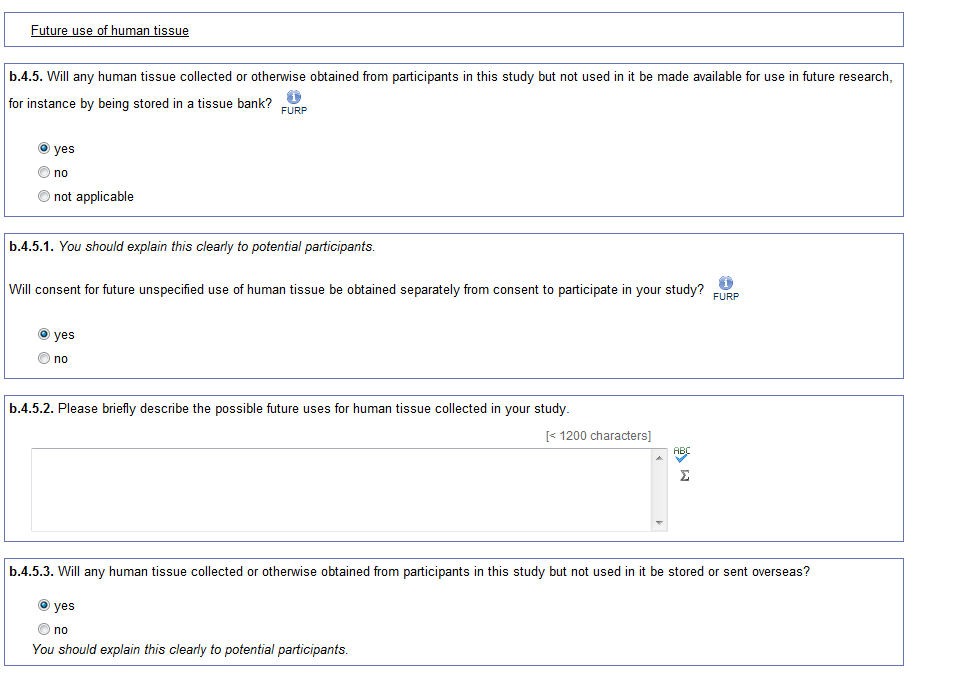
The Chair asked members to declare any potential conflicts of interest related to this application.

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

Summary of ethical issues

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

* The study is a phase III multi centre multinational study, which will involve 400 patients worldwide with approximately 3 in New Zealand.
* Participants will be randomised in a 1:1 ratio to one of two treatment arms (Arms A and B). Participants in Arm A will receive IPI145 in combination with rituximab while participants in Arm B will receive placebo in combination with rituximab.
* The Committee noted that rituximab alone is not necessarily standard practice in this setting, and that only a subset of patients would usually receive rituximab monotherapy ; rituximab is usually combined with another drug treatment. The Committee requested confirmation that this patient population was only those who can only have rituximab due to true treatment resistance or likely intolerance of combination therapy.
* Please explain how the study meets equipoise, as this question is not correctly answered in the application. The Committee understands the study is randomised between the arms, but please explain how there is genuine uncertainty between the two treatments. What evidence justifies equipoise standard?
* Please confirm that participants will not receive the experimental treatment after the study, even if it is show to be effective.
* Please note that health data derived from the study must be stored for a minimum of 10 years according to the [Health (Retention of Health Information) Regulations 1996](http://legislation.govt.nz/regulation/public/1996/0343/latest/DLM225650.html).
* Please address answers b.4.5 (Will any human tissue be collected or otherwise obtained from participants in this study but not used in it be made available for use in future research, for instance by being stored in a tissue bank?) in a cover letter. Questions below:



* The Committee requested the following changes to the Participant Information Sheet and Consent Form:
* Please include compensation sentence regarding ACC and sponsor insurance.
* Please remove any sentences that are not applicable to New Zealand.
* Please add a section on ‘what happens to my samples’ – please review the HDEC template for guidance.
* Please seek advice on what information should be included for Maori participants in relation to use of human tissue and amend PIS/CF. Please view page 15 of Te Ara Tika: Guidelines for Māori research ethics: A framework for researchers and committee members. This is accessible from the HRC website.
* Change formatting - add more white space to increase readability.
* Please address repetition.
* The Committee noted this is a poor quality PIS for the patient population.
* Add a lay language title.
* Please use formatting – bullet points.
* The Committee commended the table of adverse reactions with approximate frequencies in the PIS.
* Please clearly indicate what procedures are standard practice procedures and which are not.
* Please 16 of 19 please clarify what health information is withheld, for example can participants access their test results during the study? Please clarify what this means.

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*).
* An intervention study meets the equipoise standard if the evidence is ‘equally poised’ as to the overall balance of risks and benefits of each of the interventions offered in the study, so that it cannot be determined in advance which of the groups in a proposed study will be better off. Please explain how your study meets this standard. (*Ethical Guidelines for Intervention Studies* *para 5.18*).
* Explain what health information is not accessible if participating in the study.
* Please Address the ethical concerns raised above.
* Address missing questions in order for application to be complete.

This following information will be reviewed, and a final decision made on the application, by Ms Raewyn Idoine and Dr Devonie Waaka.

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| **7** | **Ethics ref:** | **14/STH/156** |
|  | Title: | Metformin renal handling |
|  | Principal Investigator: | Dr Dan Wright |
|  | Sponsor: |  |
|  | Clock Start Date: | 02 October 2014 |

Co-Investigator Professor Rob Walker 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.

* Prof Walker explained the study, stating that Metformin is an effective drug at controlling diabetes as it does not produce weight gain, however some people with renal impairment may be taken off metformin too early due to assumptions about absorbance mechanisms. The research team want to more accurately document ‘handling’ of metformin in people who have chronic kidney disease.
* The Committee stated that ‘renal handing’ was not easy to understand. Please use ‘kidneys’ and ‘processing’ as it is a more accurate reflection of what occurs, and what the study aims to find out. For instance ‘a study looking at how metformin is cleared from the kidneys’.
* The Committee queried if there is a formal screening process? Prof Walker stated they identify a potentially eligible person by their hospital health records, give them a PIS, bring them back to the clinic after time to consider, run a formal consent process and then when ready, start the study procedures. Prof Walker confirmed there is no additional screening as patient information is reviewed before being approached.
* The Committee requested the following changes to the Participant Information Sheet and Consent Form:
* Committee noted the PIS/CF needs to be clearer about what the study is about, at the beginning.
* Remove interpreter box.
* Incomplete sentence the end of the first page of the ICF.
* Please explain why participants are given gentamicin – and what this does. I.e. ‘this shows us how well your kidneys are working’, or ‘is a good measure of etc’.
* Please Add page numbers on the PIS/CF.
* Please make it explicit on page 1 of the ICF that participation is voluntary particularly because the treating clinician is also the researcher.
* Add ‘If you don’t take part you don’t have to give a reason and it won’t affect the care you receive’ and ‘If you change your mind mid study your treatment won’t change / you can withdraw at any time’.
* The Committee queried what happened with normal blood samples that are taken. Genetic material is explained but not the normal samples – where are these tested?
* Maori information on the PIS is on genetic but not for blood samples. Please update standard PIS/CF.
* Approved by University of Otago – please amend to Southern HDEC.
* Separate the genetic sub study – clearly mark as optional. Please review the 2007 Ministry of Health guidelines for future unspecified research.

Decision

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

* Please provide a separate Participant Information Sheet and Consent Form for the use of tissue for future unspecified research (*Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes, para 2*).
* Please amend the information sheet and consent form, taking into account the above 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 Ms Raewyn Idoine and Dr Devonie Waaka.

## 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:** | 18 November 2014, 12:00 PM |
| **Meeting venue:** | Sudima Hotel, Christchurch Airport, 550 Memorial Avenue, Christchurch |

The following members tendered apologies for this meeting.

* Mrs Angelika Frank-Alexander tendered her apologies for the December STH 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 3.10pm.