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| **Committee:** | Northern B Health and Disability Ethics Committee |
| **Meeting date:** | 05 April 2016 |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Road East, Ellerslie, Auckland |

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| **Time** | **Item of business** |
| 12:00pm | Welcome |
| 12:05pm | Confirmation of minutes of meeting of 01 March 2016 |
| 12:30pm | New applications (see over for details) |
|  | i 16/NTB/57  ii 16/NTB/50  iii 16/NTB/55  iv 16/NTB/48  v 16/NTB/63  vi 16/NTB/64  vii 16/NTB/62  viii 16/NTB/60  ix 16/NTB/61 |
| 4:45pm | General business:   * Noting section of agenda |
| 5:00pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Mrs Maliaga Erick | Lay (consumer/community perspectives) | 01/07/2015 | 01/07/2018 | Apologies |
| Mrs Stephanie Pollard | Non-lay (intervention studies) | 01/07/2015 | 01/07/2018 | Present |
| Miss Tangihaere Macfarlane | Lay (consumer/community perspectives) | 19/05/2014 | 19/05/2017 | Present |
| Mrs Phyllis Huitema | Lay (consumer/community perspectives) | 19/05/2014 | 19/05/2017 | Present |
| Mrs Kate O'Connor | Lay (ethical/moral reasoning) | 01/07/2012 | 14/12/2018 | Present |
| Dr Nora Lynch | Non-lay (health/disability service provision) | 24/07/2015 | 24/07/2018 | Present |
| Mrs Leesa Russell | Non-lay (intervention studies), Non-lay (observational studies) | 14/12/2015 | 14/12/2018 | Present |
| Mr John Hancock | Lay (the law) | 14/12/2015 | 14/12/2018 | Present |

## Welcome

The Chair opened the meeting at 12:00pm and welcomed Committee members, noting that apologies had been received from Mrs Maliaga Erick.

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 01 March 2016 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **16/NTB/57** |
|  | Title: | PREVARID- Prevention of Respiratory Infections with Vitamin D |
|  | Principal Investigator: | Associate Professor Cameron Grant |
|  | Sponsor: | University of Auckland |
|  | Clock Start Date: | 23 March 2016 |

Dr. Cameron Grant, Mrs. Tania Milne, and Dr. Teresa Gontijo 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. Children who present to Starship Children’s Hospital with a respiratory infection will be recruited for this study that investigates whether vitamin D will help prevent acute respiratory infection healthcare visits in children under 2 years old.
2. Children with a chronic condition or who already receive vitamin D will be excluded from the study.
3. Data collection involves three face-to-face interviews and two telephone follow ups.
4. Blood samples will also be collected from participants, and their parents will be asked to consent to these samples being used for future unspecified research.

Summary of ethical issues (resolved)

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

1. The Committee questioned whether it would be possible for parents to accidentally administer an overdose to their children. The Researcher explained that the dropper holds 15mls but only allows one dose at a time and an overdose could not be given accidentally.
2. The Committee questioned whether the vitamin drops have a flavour. The Researchers confirmed that they are almost tasteless.
3. The Committee noted that both the parents and their children are participants as the parents are being asked to complete questionnaires.
4. The Committee noted that no risks to the researchers were identified in the application form, however, as the study involves home visits this raises some risks to researchers. The Researchers confirmed that they will take the standard precautions with home visits, including having the researchers carry cell phones and register their visits. The Committee agreed that this is appropriate.
5. The Committee noted that the response to the question in the application form about possible cultural issues did not mention the cultural sensitivities regarding the use of human tissue. The Researchers stated that they believe, based on past experience, that participants will not raise any concerns about the use of tissue. The Committee stated that this does not mean that it is not an important cultural issue, particularly for Māori, and must be carefully explained in future applications.
6. The Committee questioned whether Māori and Pacific populations have low vitamin D levels and whether this was also a factor for other groups. For example, the Committee noted that Auckland has a large number of Asian residents who may be participants in this study. The Researcher explained that the lowest vitamin D levels they see are in Indian babies, however, in their experience Indian babies do not seem to have as many respiratory infections.

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 questioned whether tissue stored for future use would be stored in a registered tissue bank. Please provide further information regarding where the tissue will be stored. The Committee noted that if the tissue will be stored in a tissue bank in New Zealand that is not yet registered that the approval of this application will be contingent on this Tissue Bank being registered with HDEC.

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

1. The Committee queried the lack of a Māori tissue statement in the participant information sheet. The committee recommended the following statement: *“You may hold beliefs about a sacred and shared value of all or any tissue samples removed. The cultural issues associated with sending your samples overseas and/or storing your tissue should be discussed with your family/whanau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult prior to participation in research where this occurs. However, it is acknowledged that individuals have the right to choose.”*
2. The Committee noted that the participant information sheet talks about vitamin D preventing infections, however they suggest that this may be an overly strong phrasing and should be revised to clarify that vitamin D may assist with the prevention of infections. The Committee suggested that the current wording suggests that vitamin D would prevent the child needing to go to hospital for infections but there is not sufficient evidence to make this kind of claim yet.
3. Please carefully proof read the participant information sheet and consent form to reduce typographical errors and unnecessary repetition.
4. The participant information sheet explains the use of placebos but then goes on to call the placebo a study medication. Please rephrase this to reduce confusion as participants are likely to misunderstand the word ‘medication’ in this context and assume the placebo provides some benefit.
5. Please include some more information about how to give the study drops, including a picture of the dropper, in the participant information sheet.
6. Please add page numbers to the participant information sheet.
7. Please clarify that the study is paid for, funded, by Cure Kids in the participant information sheet.
8. Please rephrase the ‘What are my rights?’ section of the participant information sheet as it currently does not distinguish between the adult and children participants’ rights.
9. Please clarify in the participant information sheet what happens to the study data after the study, including how and where it is stored (in password protected computer) and who will be responsible for this data (the co-ordinating investigator).
10. Please clarify in the information sheet that study data may be used after the end of this study for future research.
11. Please remove the tick boxes from the consent form for all statements that are not truly optional, these should only be included for the statements where a participant could tick ‘no’ and still be involved in the study.
12. Please clearly name the participant information sheets and consent forms with lay titles and ensure the Future Unspecified Use of Tissue information sheet and consent form is clearly distinguished from the main information sheet and consent form.
13. Please remove the ACC statement from the Future Unspecified Use of Tissue information sheet as this is not necessary on this form.
14. Please add New Zealand contact numbers to the questionnaire.
15. Please remove the reference to another study from the questionnaire.
16. Please rephrase the question in the 6 month follow up questionnaire regarding how many drops were missed to ensure it is clear what information you are requesting.
17. Please clarify in the main information sheet that the household questionnaire will ask participants about their smoking habits, ensure it is also clear which follow ups will include this questionnaire.
18. Please include information in the participant information sheet regarding how the drops need to be stored and that they cannot be shared with others, including the participant’s other children.
19. Please clarify in the Future Unspecified Use of Tissue information sheet whether participants’ samples can be withdrawn and destroyed at a later date, please also clarify that once the samples have been used they cannot be withdrawn.

Decision

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

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*).
2. Please provide further information regarding the tissue banking arrangements for this study.

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

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| **2** | **Ethics ref:** | **16/NTB/50** |
|  | Title: | Consolidation of the Four Breast Cancer Registers |
|  | Principal Investigator: | Dr Reena Ramsaroop |
|  | Sponsor: | breast Cancer Foundation |
|  | Clock Start Date: | 17 March 2016 |

Dr Reena Ramsaroop and another researcher were present in person and another researcher attended 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 Committee noted that a number of questions in the application form are not applicable to this application as they relate to studies whereas this application is for the establishment of a national breast cancer registry.
2. Currently 4 regional registries operate independently in New Zealand and have HDEC approval to not obtain consent from patients to include their information in this registry. These registries operate on an opt-out basis and, where possible, patients are given information on the registry and how to opt-out of having their data included.
3. The Researcher explained that these registries previously obtained informed consent, however, upon review they determined that operating on this basis was producing bias results as many critical patients, such as those who died before consent could be obtained, were not included. These registries consequently applied for, and obtained, HDEC approval to operate with an opt-out consent process.
4. This application is to combine the information from these 4 registries in to one national registry.
5. The Researcher explained that currently all 4 registries operate separately in the same system and that this project would involve moving all of the information to one combined database, they hope to have this completed by the end of June 2016.
6. The Researcher explained that over 60% of patients diagnosed with breast cancer in New Zealand are currently included in these registries.

Summary of ethical issues (resolved)

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

1. The Committee questioned how many patients currently opt-out of the registries. The Researcher explained that it is much less than 1% of patients.
2. The Committee questioned how the data would be managed and governed with the new system. The Researcher explained that currently each registry has its own governance group and the proposal is to set up 1 governance group for the combined data that would include the people currently in charge of each registry and lay people. The Researcher explained that applications to use registry data would be considered by a clinician based clinical advisory group.
3. The Committee questioned who would be in charge of the transition. The Researchers explained that the head and data manager of each current registry would work together through the transition process, and throughout the transition process their existing scientific groups would continue to assess data access applications.
4. The Committee questioned whether the existing arrangements for the registries involved ongoing access to patients’ medical records. The Researcher explained that they annually follow up with patients GPs’ for an update on their progress after completing treatment and patients’ medical records are only directly accessed while they are in treatment or if they relapse or have another tumour.
5. The Committee questioned what information patients are currently given about the registry and their right to opt-out. The Researcher explained that there is a sheet of information given to patients that includes details on how to opt-out.
6. The Committee stated that patients should be offered information on the registry again if they relapse or have another tumour, to ensure they are informed that their medical records are being accessed and that their GP will be asked for annual follow up information.

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 requested further information on the proposed governance arrangements for the national registry that will result from this application. The Researchers stated that they have not yet confirmed this or developed their Standard Operating Procedures. The Committee explained that they require this information in order to make a decision to approve this application as this application essentially involves setting up a new registry.
2. The Committee questioned how many Māori representatives are will be included in the governance committee for the national registry. Please provide this information in the proposed governance structure.
3. Please explain how the new governance structure compares to the existing structure.
4. Please explain more fully how the transition will be managed and who will be in charge of governance throughout the transition process.

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

1. Please provide a pamphlet or brochure that will be given to patients to inform them of the registry and their right to opt-out. This pamphlet should be simple and include information about what health information is accessed, including that their GP will be contacted, and when ongoing data access may occur. The Researcher suggested that they can rework the Participant Information Sheet from when the registries obtained consent. The Committee noted that this may be appropriate but emphasised that this pamphlet should be easy to understand and relatively simple.
2. The Committee requested that the existing registries update their websites to reflect this change and suggest that the websites should also contain the information in the pamphlet about what information is accessed and how to opt-out.

Decision

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

1. Please provide more information on the governance structure and standard operating procedures of the new registry as well as information on the governance arrangements for the transition process
2. Please provide a pamphlet to inform patients of the registry and their right to opt-out, this pamphlet is to be given to new patients as well as those who have a relapse or new tumour and their health records will be accessed again.

This following information will be reviewed, and a final decision made on the application, by Mrs Leesa Russell and Mrs Phyllis Huitema.

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| **3** | **Ethics ref:** | **16/NTB/55** |
|  | Title: | Wellington Stroke Outcomes Study - have patient outcomes after stroke changed in 18 years? |
|  | Principal Investigator: | Dr Harry McNaughton |
|  | Sponsor: |  |
|  | Clock Start Date: | 23 March 2016 |

Dr Harry McNaughton and Dr Vivian Fu 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 Researcher explained that this is a quality assurance and improvement project and it is hoped that the results of this project will influence standard care.
2. This project involves collecting information from patients who have recently had a stroke on their quality of life and recovery outcomes 6 – 9 months post stroke.

Summary of ethical issues (resolved)

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

1. The Committee questioned whether the exact same information would be collected from the new participants as was collected from the 1997 historical control participants. The Researcher explained that one extra bit of information would be collected from new participants but that otherwise it would be the same information.
2. The Committee questioned whether the 1997 study had the same follow up periods. The Researcher explained that the 1997 study followed up with participants at 6 and 12 months post stroke but found no difference between these, therefore, the researchers feel that there is not a benefit from waiting to do a 12 month follow up and have chosen 6 and 9 months as the follow up points instead.
3. The Committee noted the reference to a 2013 study that compared 100 patients to the 1997 data, and another current intervention study. The Committee questioned the relationship between this intervention study and the observational study being applied for. The Researcher explained that participants from both studies would be recruited from the same group and it was expected that some participants would be involved in both studies.
4. The Committee questioned the recruitment criteria for this study. The Researcher explained that 250 patients who have had a stroke in the 6 months prior to the study commencing would be recruited as the study required additional follow up at 6 and 9 months post stroke.
5. The Committee questioned whether Victoria University are the sponsor for this study as this study is being conducted by a PHD candidate. The Researcher explained that this study is for a HRC Medical Research Institute fellowship, and another study is being conducted for the purposes of the PHD, consequently the Medical Research Institute are the sponsor for this study.
6. The Committee questioned when and how participants would be invited to participate. The Researcher explained that the participant information sheet and consent form will be posted to participants and 10-14 days following this a researcher will phone participants to obtain consent.
7. The Committee questioned whether possible culturally appropriate methods of data collection had been considered for Māori or Pacific participants. The Researchers explained that they have a number of good resources available to them such as training and interpreters and hope to be as culturally sensitive as possible.

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 proposed consent process involves obtaining oral consent rather than written consent and questioned the appropriateness of this given that these participants may have diminished intellectual capacity or reduced communication capabilities due to their stroke. The Committee requested further information on how oral consent would be documented and further justification of why this was necessary for this study.
2. The Committee questioned whether the historical comparator group, who were involved in a 1997 study, consented to their data being used in future research. The Researcher explained that while these participants were consented to go into the 1997 study they believe that it is unlikely that the consent process would have included being asked to consent to the future use of their data as this was not common at the time. The Committee noted that it would be good to confirm this.
3. The Committee noted that some participants may have a reduced ability to provide informed consent due to their stroke and questioned how capacity to consent would be determined and documented. The Researcher stated that it was their intention to include anyone who seemed to understand the study and who could provide meaningful answers to the researcher’s questions when phoned. The Committee requested further information on how capacity to consent would be measured and determined, suggesting that the use of a standardised measure may be appropriate.
4. The Committee noted that some participants may not be able to provide consent over the phone due to a communication difficulty, however, are capable of providing consent. The Committee stated that they required further information on how this situation would be handled.
5. The Committee referenced the participant’s right to give consent with support, in reference to those with communication difficulties. The Researcher explained that they hoped that the letter sent out to potential participants would also help to inform their family or other support people, as they expected those with communication or other issues to not be living alone. The Committee stated that they were not confident that this would be the case. The Researcher stated that some participants would live in assisted living facilities and they would be able to discuss the participant’s ability to consent with the staff from the facility. The Committee appreciated that this was a possibility but requested more formal documentation of the proposed consent procedures and requirements for this study.
6. The Committee questioned when the participant’s family are consulted whether they will complete a different consent form and questionnaire, on their views of their family member’s outcomes and recovery, or if they would be asked specifically to provide health information on behalf of the participant. The Researcher confirmed that if the participant was unable to provide consent themselves that they intended to ask their family members to provide consent and to give them the requested health information on behalf of the participant. The Committee stated that in New Zealand it is not acceptable to have proxy consent to participation in research and that it is not permissible to obtain health information for research from someone who is not the participant themselves.
7. The Committee noted that this application includes a number of ethically relevant aspects, primarily regarding consent. To proceed with approval of this study the committee require further information on how these are addressed, including clarity of consent processes in the study protocol. These include:
   * Accessing health information and study data from the 1997 study participants without clarity regarding if they consented to their data being used for future research. The Committee noted that it is possible for them to approve retrospective access to health information without consent, however, it is unclear whether this is the case for these participants or whether these participants provided consent to the use of their data in future studies.
   * Accessing health information from patients who have had a stroke in the past 6 months in order to send them participant information sheets and consent forms and to follow up by phone with these patients to obtain consent.
   * The possibility that some participants will have a diminished capacity to give valid informed consent due to their stroke. The Committee stated that they require clarity regarding how capacity to consent would be determined.
   * The Committee noted that for participants unable to provide informed consent to be included in research they must be recruited under Right 7(4) of the HDC code of rights, however, this requires that participation in the study is in the best interests of the participant and the Committee stated that it is difficult to see how this would be demonstrated for a prospective observational study. Consequently, the Committee requested further information about whether participants unable to consent would be excluded from the study, or how the inclusion of non-consenting participants meets Right 7(4) of the HDC Code of Rights.
   * The proposal to obtain proxy consent from participant’s family members if the participant is unable to provide informed consent on their own behalf. The Committee noted that it is not legally acceptable in New Zealand for someone to provide consent on behalf of another adult for the purpose of research. Please alter the study documents to reflect this.
   * Obtaining oral rather than written consent. The Committee stated that they require more information on how this will be documented and the reasons consent would not be obtained in a written form and why oral consent was considered appropriate in this case.
   * Please justify the reasons that participants with diminished communication capabilities will be excluded from the study, as they may be able to provide informed consent but unable to communicate this over the telephone.
8. The Committee noted that due to the complex issues raised regarding consent in this population group, specifically regarding collecting additional information from participants who may lack the capacity to provide informed consent, that the Committee require further justification regarding why this study could not be completed another way. For example, by only including routinely collected health information that can be accessed retrospectively, as this method could be approved by the HDEC if they believe the benefits of the study outweigh the loss of privacy. Whereas, the inclusion of non-consenting participants in a prospective study requires that the inclusion of these participants meets Right 7(4) of the HDC Code of Rights.
9. The Committee noted a reference to a summer student project that collected information from 20 stroke patients without HDEC approval as it was determined to be outside HDEC scope of review. Please provide further information about this project including what information was collected, how it was determined if participants were competent to provide informed consent, and whether the same participants will be approached for this study.

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

1. Please add information to the Participant Information Sheet on how participants can opt-out of being phoned by the researchers.

Decision

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

1. The requirement for informed consent (Ethical Guidelines for Observational Studies section 6 and HDC Code of Rights Right 7(4)).

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| **4** | **Ethics ref:** | **16/NTB/48** |
|  | Title: | STUDY OF THE INVESTIGATIONAL DRUG AVELUMAB IN PATIENTS WITH ADVANCED RENALCELL CARCINOMA |
|  | Principal Investigator: | Dr Alvin Tan |
|  | Sponsor: | Pfizer Australia/NewZealand |
|  | Clock Start Date: | 17 March 2016 |

Dr Alvin Tan 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. This is a multinational phase 3 trial of the drug Avelumab in patients with advanced renal cell carcinoma.
2. 3-5 participants will be recruited from each site in New Zealand, it is currently expected that New Zealand will have 3 sites.

Summary of ethical issues (resolved)

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

1. The Committee questioned whether SCOTT approval is being sought for this study. The Researcher confirmed that this is currently underway.
2. The Committee questioned whether participants must have an already stored tissue sample to be involved in this study. The Researchers explained that participants must already have a sample that can be used or agree to have a new biopsy.

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 protocol includes information about proxy consent and, although this is an international protocol that is also for countries that allow proxy consent, it must be clear that it is not acceptable to have proxy consent for research in New Zealand.
2. The Committee noted that there is a chance that it will be discovered that participants have a genetic disorder, however it is not intended to tell these participants about this if it is discovered. The Committee stated that if it is possible to identify the participant that they should be informed of any clinically significant findings. Please clarify whether participants will be informed of any unexpected findings or not and ensure that the Participant Information Sheet reflects this.
3. The Committee noted that the information sheet states that participants will be informed of the results of the study, however as they have advanced renal cell carcinoma they may not survive long enough to be informed of study results. Please clarify whether their next of kin will be informed of the study results.
4. Please confirm whether the study sponsor will offer ACC equivalent compensation. In the event of injury to a participant in your intervention study, will compensation potentially be available for all of the following entitlements, which would be available through ACC: rehabilitation (comprising treatment, social rehabilitation, and vocational rehabilitation), first week compensation, weekly compensation, lump sum compensation for permanent impairment, funeral grants, survivors' grants, weekly compensation for the spouse or partner, children and other dependents of a deceased claimant, and child care payments.

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

1. The Committee questioned where samples are being sent overseas. The Researcher stated that they are being sent to the sponsor’s central lab. Please clarify where in the world this is and state in the participant information sheet which country samples will be sent to.
2. Please clarify in the participant information sheet what will happen to participant’s tissue if they do not consent to Future Unspecified Use of Tissue, for example that this tissue will be disposed of.
3. Please state that tissue stored in an overseas tissue bank for future research will not be subject to New Zealand ethics approval or regulation.
4. Please use Statistics New Zealand's ethnicity classifications when collecting ethnicity data to ensure the options available are suitable for New Zealand participants. These classifications are: New Zealand European, Māori, Samoan, Cook Islands Māori, Tongan, Niuean, Chinese, Indian, and Other (such as Dutch, Japanese, Tokelauan) please state.
5. The Committee noted that the participant information sheet is difficult for lay participants to understand and includes a lot of technical terms. The Researcher responded that they have already worked on improving this form and would rework it again to help improve readability. The Committee stated that the participant information sheet exists to inform participants about what their participation involves and as such it is essential that it is able to be understood by participants.
6. Please ensure it is clear in the participant information sheet whether participants will be able to get access to the study drug after the end of the trial, or if they will only continue to have access if they are enrolled in the rollover study.
7. The protocol details the risks from IV infusion but this information is not in the participant information sheet, please ensure this is included in both.
8. Please add New Zealand contact numbers to the patient emergency card as a hyperlink is not suitable.
9. Please clarify in the participant information sheet why participants will be given paracetamol.
10. Please include information about the potential cultural issues with genetic information in the participant information sheet.
11. The participant information sheet states that information will be safeguarded overseas, please be more specific about how it will be safeguarded.
12. Please ensure the each optional aspect of the study has a separate consent form.
13. Please add a lay title to each participant information sheet and consent form.
14. Please review forms to ensure that Americanisations are removed, such as American spelling.
15. Please ensure Māori Health / cultural support contact details are included in the Participant Information Sheet.
16. Please change ‘consult with a kaumatua’ to ‘consult with whanau and/or kaumatua’.
17. Please change ‘and’ to ‘and/or’ in the section: ‘xxx respects the importance of these values and beliefs so please inform us if you wish to have whanau support present **and/or** perform a karakia when donating this blood sample’.
18. The Pregnant partner form states ‘we have been informed that you have become pregnant’ please clarify who has informed you of this.
19. Please clarify if participants or their family will be informed of the study results.
20. Please rephrase page two of the participant information sheet as it currently suggests that participants can die twice as they are investigating whether the participant will survive longer in one study arm or the other.
21. Please thoroughly proof read all participant facing documents to reduce typographical errors.
22. Please improve lay readability of all participant facing documents.

Decision

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

1. Please respond to the outstanding ethical concerns outlined above.
2. 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 Mrs Leesa Russell and Mrs Kate O’Connor.

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| **5** | **Ethics ref:** | **16/NTB/63** |
|  | Title: | M13-542 A study comparing ABT-494 to Placebo in subjects with moderately to severe Rheumatoid Arthritis with Inadequate response to Biologic Disease Modifying Anti-Rheumatic Drugs (bDMARDS) |
|  | Principal Investigator: | Dr Daniel Ching |
|  | Sponsor: | AbbVie Pty Ltd |
|  | Clock Start Date: | 23 March 2016 |

Dr Daniel Ching 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 (outstanding)

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

1. Please clarify who the locality is for this study. The Committee noted that section 10 of the HDEC Standard Operating Procedures defines the locality as an organisation responsible for a hospital, health centre, surgery or other establishment or facility in New Zealand at or from which the procedures outlined in the protocol of a study are to be conducted. In this case the study is being conducted by a private company in space rented from the District Health Board, please clarify whether the DHB will be providing locality authorisation as they are responsible for the hospital at which the study procedures will be conducted.
2. Please confirm how potential participants will be identified and recruited for the study.

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

1. Please clarify in the participant information sheet which medications participants must stop taking while in this study. It is essential it is clear to participants that their involvement in this study precludes them from other possible treatments, although, the Committee noted that it is an inclusion criteria of the study that participants must be failing to respond to alternative treatments.
2. Please clarify in the participant information sheet which medications participants must stop taking 24 hours before each study visit.
3. The Committee noted that some steroid injections that participants may receive as part of standard care are prohibited during the study, and if participants require these they may be withdrawn from the study. Please ensure this is clear in the participant information sheet.
4. Please clarify in the participant information sheet whether participants may be withdrawn from the study if they have a disease flare that cannot be managed with allowable medications.
5. Please add a lay title to the participant information sheet.
6. The participant information sheet states that if the recruitment target has been met that potential participants who have completed screening will not be enrolled in the study due to the competitive enrolment. However, the Researcher has confirmed that the recruitment target is not strict and that potential participants who are at the end of enrolment when the target is reached will still be able to participate in the study. Please amend this section to reflect this.
7. Please adjust the page numbers on the participant information sheet as currently it restarts part way through the document. Please also ensure the length of the document stated on the first page is updated for accuracy.
8. Please explain the abbreviations used in the tables in the Participant Information Sheet, for example please state that BL means Baseline Information.
9. Please ensure that the participant information sheet uses New Zealand spelling throughout.
10. Page 9 of the participant information sheet refers to US law, please remove this reference and adjust for relevancy to New Zealand law.
11. The reproductive risks sections of the participant information sheet is overly complicated. Please revise this section to only include the information participants need to know in a simple and easy to understand way.
12. Please clarify when reimbursement is paid, for example if it is paid at each visit.
13. Please specify what is meant by a reasonable amount of reimbursement, how this is calculated, and whether there is a cap that may exclude participants who live far away from the study site.
14. Please clarify in the participant information sheet that although participants have a right to access information collected about them at all times, if they wish to access study information prior to unblinding they may need to be withdrawn from the study.
15. Please clarify in the participant information sheet that study data will be sent overseas and not covered by New Zealand regulation or review. Please specify where in the world this information may be sent.
16. Please clarify that participants will not be informed of the results of the optional pharmacogenomics aspect of the study.
17. Please clarify when and if participants can withdraw their samples from the Future Unspecified Use of Tissue aspect of this study. The Committee notes that if it is possible to identify and withdraw tissue that participants should be allowed to do so if they change their mind.
18. Please clarify whether identifiable information will be sent with tissue being stored for Future Unspecified Use of Tissue. The Committee notes that tissue samples should have identifiers, such as their name or address, removed before being sent overseas whenever possible.
19. The pregnant partner information sheet states that they need to withdraw in writing, please remove this as this is not a requirement, verbal withdrawal is legally binding in New Zealand.
20. In the Future Unspecified Use of Tissue information sheet please remove the ACC compensation information rather than referring to the main information sheet.
21. Please ensure all relevant contact information is included, such as a Māori cultural support person.
22. Please update the patient contact card with New Zealand contact information.
23. Please clarify that for participants to continue in to phase 2 of this study they need to improve a certain amount in phase 1 of the study.
24. Please state in the participant information sheet what happens after the study ends, specifically that it is not known whether participants will be able to access the study drug after the end of the study.

Decision

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

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*).
2. Please respond to the outstanding ethical concerns detailed above.

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

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| **6** | **Ethics ref:** | **16/NTB/64** |
|  | Title: | Persistent airflow limitation and the airway microbiome in childhood asthma |
|  | Principal Investigator: | Prof Jeroen Douwes |
|  | Sponsor: | Massey University |
|  | Clock Start Date: | 23 March 2016 |

Dr Jeroen Douwes 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 Committee thanked the researchers for the well written application on an important topic and congratulated them on receiving HRC funding.
2. The Committee noted that good evidence of the peer review process had been provided.

Summary of ethical issues (resolved)

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

1. The Committee questioned how participants would be identified. The Researchers explained that GPs will be approached and informed of the study and asked to send an invitation letter to any of their patients who they feel would be suitable for the study. The Researcher also noted that a previous study had recruited participants directly by accessing their medical records and stated that this was their backup plan if recruitment through GPs was not successful. The Committee noted that if it was decided to approach participants directly then an Amendment should be submitted for HDEC approval, the Researcher agreed and stated that this was their plan.
2. The Committee questioned whether following the sending of the invitation letter if interested parents would need to phone the researchers for more information or to enrol. The Researcher confirmed that interested parents would phone the researchers and be sent a participant information sheet as well as discussing the study over the phone with the researchers.
3. The Committee noted that participants are children 8-17 years old and that any participants aged 16 or over must provide their own consent, and younger participants who are deemed competent to provide informed consent should be asked to do so. For younger participants unable to provide their own informed consent, their parent or guardian must provide informed consent on their behalf and the child must provide assent.
4. The Committee questioned whether the researchers believe they have suitably addressed the concerns raised in the peer review. The Researcher stated that they believe they have adequately rebutted these comments in the rebuttal provided to the committee.
5. The Committee questioned the question regarding suicide in the questionnaire. The Researcher stated that this question was included as a means of measuring the stress levels of participants. The Committee stated that they did not believe this question is suitable or appropriate, especially as it asks for the name of this person or their relationship to the child, and request that it is removed. The Committee suggested that another standardised and validated stress measurement question or tool would be suitable to include.

Summary of ethical issues (outstanding)

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

1. Please add a statement to the start of the invitation letter about the voluntary nature of participation, this statement is already at the bottom of the letter and should be included at the top and bottom of the letter.
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. Please also provide a re-consent form for any participants who turn 16 during your study and initially provided assent. The Committee noted that due to the short duration of the study that this may not apply to any participants, however, if this is the case please confirm that all participants who are at least 16 at the time of consent or will turn 16 during the study will provide fully informed consent, rather than assent at the time of recruitment.
4. Please provide a separate information sheet and consent form for Future Unspecified Use of Tissue. The Committee emphasised that there is a HDEC template for these forms and to please include the information outlined in the template when developing these forms.
5. The Committee noted that for the storage of tissue for future unspecified use that if it would be possible for this tissue to be withdrawn, such as if some identifiable information is retained with this tissue, that participants who did not provide informed consent to the initial storage of this tissue (because they were children and consent was obtained from their parents) should be asked to re-consent to the continued storage of this tissue when they turn 16. Please either provide a suitable information sheet and consent form for this or confirm that no identifiable information will be retained with tissue samples (including a study number that could be linked to an individual participant) and that once collected tissue samples cannot be withdrawn from storage at a participant’s request.
6. The Committee stated that the collection of hair samples for this study raises cultural sensitivities due to the head being considered tapu (sacred) by Māori. Please acknowledge this in the participant information sheet.
7. Please clarify in the information sheet how study data will be stored during, not just after, the study.
8. Please proof read the participant information sheet to reduce typographical errors.
9. Please ensure that the information sheets are consistent regarding the number of participants.
10. For the protection of the child’s privacy please do not collect the child’s name on the questionnaire. This form already collects the child’s study number and can be linked to their name for contacting their GP when and if required.
11. Please use Statistics New Zealand's ethnicity classifications when collecting ethnicity data to ensure the options available are suitable for New Zealand participants. These classifications are: New Zealand European, Māori, Samoan, Cook Islands Māori, Tongan, Niuean, Chinese, Indian, and Other (such as Dutch, Japanese, Tokelauan) please state.
12. Please ensure it is clear in the parent information sheet that you are referring to ‘your child’ rather than to the parent themselves.
13. Please ensure the information sheets for parents and participants consenting for themselves includes the ACC compensation information, the Committee suggests the wording from the HDEC template may be a useful guide.
14. Please ensure it is clear in the Future Unspecified Use of Tissue information sheets whether participants can request information on the analysis of their samples.
15. Please add a place to the consent forms for the member of the research team who has explained the project to declare that they believe the participant understands the study and has given informed consent to participate, or for their child to participate in the case of the parent consent forms.
16. The Committee noted that participants do not need to give a reason for their withdrawal from the study, nor do they need to withdraw in writing as verbal withdrawal is legally binding in New Zealand. Please add an option to the reasons for withdrawal that participants can select if they do not want to give a reason, and also ensure it is clear that written withdrawal is not mandatory.
17. The Committee queried the lack of a Māori tissue statement in the participant information sheet. The committee recommended the following statement: *“You may hold beliefs about a sacred and shared value of all or any tissue samples removed. The cultural issues associated with sending your samples overseas and/or storing your tissue should be discussed with your family/whanau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult prior to participation in research where this occurs. However, it is acknowledged that individuals have the right to choose.”*
18. Please include the name and title of the Māori cultural contact person who can be contacted about the study.
19. Please remove the question about suicide from the Phase 2 questionnaire.

Decision

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

1. 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 Mrs Stephanie Pollard and Miss Tangihaere Macfarlane.

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| **7** | **Ethics ref:** | **16/NTB/62** |
|  | Title: | PLUS Study - Plasma-Lyte 148® versus Saline Study |
|  | Principal Investigator: | Dr Paul Young |
|  | Sponsor: | The George Institute |
|  | Clock Start Date: | 23 March 2016 |

Dr Paul Young and 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. The Researchers stated that this is a fairly standard comparative effectiveness study that is similar to many others that have been conducted.
2. Approximately 8800 patients will be recruited for this study worldwide, 1500 in New Zealand, over the next 3 years, and the primary outcome is 90 day mortality.
3. This study will compare Saline to Plasma-Lyte 148 in critically ill patients requiring fluid resuscitation.
4. All participants in this study require fluid resuscitation and will be randomised to receive one of these two fluids.
5. Both Plasma-Lyte 148 and saline are approved and commonly given to ICU patients in New Zealand in usual clinical practice and this trial is designed to compare the effectiveness of these standard treatments.
6. Many participants in this study will be recruited without consent as they are critically ill and unable to provide informed consent.
7. The Committee stated that they appreciated the thorough cover letter included with this application that provided detailed responses to many of the potential ethical concerns raised by this study, including how it meets Right 7(4) of the HDC Code of Rights.
8. Some participants in this study will well enough to provide informed consent to participate prior to enrolment, others will not be able to provide consent prior to enrolment but will recover sufficiently to be informed that they were enrolled in a study and provide consent to their data being included in the study, other participants will never recover sufficiently to be informed of the study or provide informed consent.
9. For participants unable to provide informed consent, where possible, the researchers will consult with the participant’s family or other suitable persons regarding their views of whether the participant would want to be involved in the study if they were able to provide informed consent, consistent with Right 7(4) of the HDC Code of Rights.
10. In all cases, participants will only be enrolled in the study and randomised to one of the study treatment arms if their treating clinician believes that study enrolment is in the best interests of the individual participant, consistent with Right 7(4) of the HDC Code of Rights.

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 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. The Committee asked the researcher to confirm that it was their clinical judgement that study participation would be in the best interests of each participant. The Researcher stated that this was their professional opinion.
2. The Committee questioned whether the participant’s family would be consulted about the inclusion of their data if the researchers were unable to consult the family prior to enrolling the participant in the study intervention, and the participant had not recovered sufficiently to be asked themselves to provide consent. The Researcher explained that although they would take reasonable steps to consult the participant’s family prior to administering the intervention, they felt that if this had not been possible that approaching the participant’s family regarding their views of whether the participant would want their data included in the study would be unnecessarily distressing for the family as they may have just lost a close family member, and the intervention would have already occurred. The Committee agreed with this sentiment and the decision to only consult with the participant’s family or other suitable person if this could be done prior to enrolling the participant in the intervention aspect of the study.
3. The Committee noted that it is essential that participant’s family do not perceive that they are giving consent on behalf of the participant, rather, they must understand that they are being consulted on their views of whether the participant would agree to be in the study if there were able to provide consent.
4. The Committee questioned whether the study involved only routinely collected health information. The Researcher explained that for participants who were unable to provide informed consent, such as those who die, that only routinely collected information would be used. Participants who survive and are able to provide informed consent will have extra information collected in the form of a questionnaire.

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

1. Please ensure the consent form contains all of the relevant information from the HDEC template, including that the participant has had sufficient time to consider their participation.
2. Please add a section to the participant information sheet to reflect the rights of participants recruited without consent. This section should include that the participant was recruited as their treating clinician enrolled them because they believed it was in their best interests, but that they retain the right to withdraw their data from the study and not agree to further participation.

Decision

This application was *approved* by consensus, subject to the following non-standard conditions.

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).

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| **8** | **Ethics ref:** | **16/NTB/60** |
|  | Title: | Comparison of the blood levels of two forms of imatinib tablet in healthy male volunteers under fed conditions |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Natco Pharma Australia Pty Ltd |
|  | Clock Start Date: | 23 March 2016 |

Dr Noelyn Hung, Dr Tak 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. This is a bioequivalence study of two forms of imatinib tablet in 24 health male volunteers.
2. The Committee appreciated the high quality of this application.

Summary of ethical issues (resolved)

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

1. The Committee questioned the data safety monitoring arrangements for this study. The Researchers confirmed that they have internal data safety monitoring and study data will be reviewed between each study period.
2. The Committee questioned whether the benefits in this study are proportional to the risks, given that this study involves healthy volunteers. The Researchers confirmed that they have no safety concerns for this study as the safety of this medication is well tested.
3. The Committee questioned whether the researchers will obtain a medical history of participants. The Researchers stated that they do not usually obtain formal medical records, instead they have a series of questionnaires that they go through with the participants and if any specific concerns are highlighted they will follow up with the participants GP. These questionnaires are done more than once to ensure participants give consistent responses. Participants also have blood tests and drug of abuse screening. The Researcher assured the committee that they have enough medical information on participants and are confident in the reliability of this information, and they are confident that they can identify any participants who may be lying to try meet study criteria.
4. The Committee questioned whether the researchers believe that the reimbursement offered to participants is suitable. The Researcher stated that they use the same calculation for all of their studies that have been approved in the past and feel that this is suitable.

Summary of ethical issues (outstanding)

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

1. Please be clear in the participant information sheet that study participants must use condoms for the whole study period with all sexual partners.
2. Please add a statement to the participant information sheet that participants must use condoms, and not donate blood or semen.
3. Please remove the tick boxes from the consent form as these suggest that each statement is optional even though only a ‘yes’ tick box is included.
4. Please remove the reference to PAYE in the participant information sheet and confirm the appropriate tax information to include, the Committee suggested that it may be Withholding Tax but the Researchers should confirm their tax situation.

Decision

This application was *approved* by consensus, subject to the following non-standard conditions.

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*).

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| **9** | **Ethics ref:** | **16/NTB/61** |
|  | Title: | Comparison of the blood levels of two forms of buprenorphine 20 mcg/hr transdermal patch in healthy male and female volunteers over 22 days in each study period |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Juno Pharmaceuticals Pty Ltd |
|  | Clock Start Date: | 23 March 2016 |

Dr Noelyn Hung, Dr Tak 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 Committee appreciated the high quality of this application.
2. This study involves the comparison of the blood levels of two forms of buprenorphine 20mcg/hr transdermal patch in healthy male and female volunteers.
3. Participants will also receive an opioid blocker to stop the effects of the study drug, including the unpleasant side effects.

Summary of ethical issues (resolved)

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

1. The Committee questioned the data safety monitoring arrangements for this study. The Researchers confirmed that they have internal data safety monitoring and study data will be reviewed between each study period.
2. The Committee questioned whether the researchers will obtain a medical history of participants. The Researchers stated that they do not usually obtain formal medical records, instead they have a series of questionnaires that they go through with the participants and if any specific concerns are highlighted they will follow up with the participants GP. These questionnaires are done more than once to ensure they give consistent responses. Participants also have blood tests, and drug of abuse screening. The Researcher assured the committee that they have enough medical information on participants and are confident in the reliability of this information and they are confident that they can identify any participants who may be lying to try meet study criteria.
3. The Committee questioned whether the researchers believe that the reimbursement offered to participants is suitable. The Researcher stated that they use the same calculation for all of their studies that have been approved in the past and feel that this is suitable.

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 questioned how the risk of addiction would be managed in this study. The Researcher explained that the opioid blocker would help to reduce the addictive nature of the study drug and that participants’ blood would be monitored to ensure that the opioid blocker is being taken as directed.
2. The Committee asked for further information on how addiction risk would be managed in this study. The Researchers mentioned a German study that successfully managed the risk of addiction with this drug and opioid blocker. The Committee requested further information on this German study.
3. The Committee questioned whether the drug of abuse screening would pick up on synthetic drugs and asked the researchers to confirm the answer to this question.

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

1. Please be clear in the participant information sheet that study participants must use condoms for the whole study period with all sexual partners.
2. Please add a statement to the participant information sheet that participants must use condoms, and not donate blood or semen.
3. Please remove the tick boxes from the consent form as these suggest that each statement is optional even though only a ‘yes’ tick box is included.
4. Please remove the reference to PAYE in the participant information sheet and confirm the appropriate tax information to include, the Committee suggested that it may be Withholding Tax but the Researchers should confirm their tax situation.
5. Please add a statement to the participant information sheet advising participants that their blood will be tested to ensure they are taking the opioid blocker and not misusing the patch and that if it is discovered that they are not following the study requirements they will be removed from the study.

Decision

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

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*).
2. Please respond to the Committee’s outstanding ethical concerns detailed above.

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

## 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:** | 03 May 2016, 12:00 PM |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Road East, Ellerslie, Auckland |

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 5:00pm.