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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 10 November 2015 |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Auckland |

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| **Time** | **Item of business** |
| 1.00pm | Welcome |
| 1.05pm | Confirmation of minutes of meeting of 13 October 2015 and 21 October 2015. |
| 1.30pm | New applications (see over for details) |
| 1.30-1.55  1.55-2.20  2.20-2.45  2.45-3.10  3.10-3.35  3.35-4.00  4.00-4.25  4.25-4.50  4.50-5.15  5.15-5.40  5.40-6.05  6.05-6.30 | i 15/NTA/168  ii 15/NTA/169  iii 15/NTA/170  iv 15/NTA/171  v 15/NTA/172  vi 15/NTA/173  vii 15/NTA/174  viii 15/NTA/175  ix 15/NTA/176  x 15/NTA/183  xi 15/NTA/184  xii 15/NTA/185 |
| 6.30pm | General business:   * Noting section of agenda |
| 6.30pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Brian Fergus | Lay (consumer/community perspectives) | 01/07/2012 | 01/07/2015 | Present |
| Ms Susan Buckland | Lay (consumer/community perspectives) | 01/07/2012 | 01/07/2015 | Present |
| Mr Kerry Hiini | Lay (consumer/community perspectives) | 01/07/2012 | 01/07/2015 | Present |
| Dr Karen Bartholomew | Non-lay (intervention studies) | 01/07/2013 | 01/07/2016 | Apologies |
| Dr Christine Crooks | Non-lay (intervention studies) | 01/07/2013 | 01/07/2015 | Present |
| Mr Mark Smith | Non-lay (intervention studies) | 01/09/2014 | 01/09/2015 | Apologies |
| Mrs Kate O'Connor |  |  |  | Present |
| Ms Shamim Chagani | Non-lay (health/disability service provision) | 01/07/2012 | 01/07/2015 | Present |

## Welcome

The Chair opened the meeting at 1pm and welcomed Committee members, noting that apologies had been received from Dr Karen Bartholomew and Mr Mark Smith.

The Chair noted that fewer than five appointed members of the Committee were present, and that it would be necessary to co-opt members of other HDECs in accordance with the SOPs. Mrs Kate O’Connor (Northern B) confirmed her eligibility, and was co-opted by the Chair as member of the Committee for the duration of the meeting.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

## Confirmation of previous minutes

The minutes of the meeting of 13 October 2015 and 21 October 2015 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **15/NTA/168** |
|  | Title: | Pulse oximetry screening feasibility study |
|  | Principal Investigator: | Prof Frank Bloomfield |
|  | Sponsor: | University of Auckland |
|  | Clock Start Date: | 29 October 2015 |

Dr Elza Cloete was 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 the study

1. The Pulse oximetry is a hand-held, non-invasive, safe and easy-to-use device that gives

important information about vital signs and oxygen saturation level. The researcher explained that the device has been in use for many years. It is valuable in an ICU setting as it gives continuous monitoring. It is used as screening tool to detect congenital heart defects.

1. Current screening strategies to detect congenital heart defects in New Zealand include physical examination and antenatal ultrasound. Mid-trimester foetal anatomy scans are offered to all pregnant women in New Zealand. The use of antenatal ultrasound screening to detect congenital heart disease has a sensitivity ranging between 50-80% and the proportion of congenital heart defects detected antenatally in New Zealand is 46%. The main focus of this study is on feasibility but the research team will also check the specificity and sensitivity of the device.
2. A recent retrospective study reviewing cases of major congenital heart disease in New Zealand over a five year period estimated that 15 babies will receive a late diagnosis of critical CHD and that 4 will die as a result. The device is likely to detect more than 50% of these infants, reducing the risk of death. It has been shown that the use of this device in conjunction with antenatal screening can diagnose 96% of babies with congenital heart defects.
3. The researcher explained that the rest of world has been screening for many years now and this is nothing new. For the research team, the question is about feasibility of a screening programme within the NZ maternity setting, which is largely midwifery focused. The researchers would like to know whether it is possible for NZ to have a uniform nationwide screening programme and essentially look at application within the NZ context and fit in with healthcare providers.
4. The committee queried whether the researchers will also carry out ultrasound screening as part of this study. They will not. The researcher explained that women have antenatal screening and once a baby delivered it is part of routine to do a physical examination as standard of care. The use of the device is additional.

Summary of ethical issues (resolved)

1. The committee queried whether the researchers were concerned about the risk of false positives. It was noted that the likelihood of a false positive measurement is minimal but in saying so a false positive result has the added benefit of diagnosing diseases other than congenital heart disease (e.g. sepsis, pneumonia). The researcher noted that the number affected is insignificant and a false positive test will usually delay discharge in one or two babies a year.
2. The researcher confirmed for the committee that they would measure anxiety levels with an anonymous survey especially for those with positive results. The committee noted that the questions on the survey included with the application didn’t appear to be related to anxiety and discussed whether it would be a valid way of assessing anxiety. The committee suggested that the research team may wish to refer to a standard questionnaire on assessing anxiety.
3. The committee asked whether the researchers were expecting any differences across facilities. The researcher confirmed that they are and they will be interested to see whether clinician workload differences would make a difference.
4. The researcher confirmed that the research team has consulted with Helen Wihongi and that they were not required to make changes to the study following the consultation.

Ethical issues (outstanding)

1. The committee noted that the researchers are not intending to seek written consent from parents/caregivers. The researcher explained their standard treatment consent process noting that they seek verbal consent. She noted that other studies have reported that written consent can contribute to anxiety. The committee explained that as the research team will be collecting data they would like to see that the information on the participant information sheet has been explained to parents and that they have given signed consent. Given the low risk associated with this study, the committee agreed that provision be made for the participants to sign at the end of the information sheet (rather than have a separate CF), that includes a statement that the participants have had the information explained to them and that they understand what is involved in the study.

The committee requested the following changes to the participant information sheet:

1. In order to improve understanding by the mothers, the committee suggested an opening sentence explaining why you are doing the study – i.e. that babies are screened at 35 weeks and have a physical examination at birth and that the pulse oximetry is an additional procedure. The committee suggested the inclusion of a photo of the pulse oximeter.
2. Please review the formatting of the document.
3. Please include research team contact details so that participants can contact you if they change their mind about being in the study.
4. Please include the following clause about access to make a claim for compensation. “If you were injured in this study, which is unlikely, you would be eligible **to apply** for compensation from ACC just as you would be if you were injured in an accident at work or at home.”
5. Please include provision for the participants to sign at the end of the information sheet that includes a statement that the participants have had the information explained to them and that they understand what is involved in the study.

Decision

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

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| **2** | **Ethics ref:** | **15/NTA/169** |
|  | Title: | The LaP Study |
|  | Principal Investigator: | Dr Jane Alsweiler |
|  | Sponsor: | The University of Auckland |
|  | Clock Start Date: | 29 October 2015 |

Dr Jane Alsweiler was 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 the study

1. The researcher explained that this is a study looking at low blood pressure in babies born at 34-36 weeks. Babies born 4-6 weeks early have a higher risk than babies born at term, of having developmental delay. It is not known why they may be at higher risk. The researchers are looking to improve outcomes for these babies.
2. Babies born very preterm, often have brief periods when their oxygen saturation drops below normal. It is common for them to have a pause in breathing (apnoea) and this is effectively treated with caffeine (in normal practice). It is possible that babies born 4-6 weeks preterm may also have dips in oxygen. This study will look at oxygen levels in late preterm babies and compare their oxygen with babies born at full term. The babies will have an overnight pulse oximetry to measure oxygen levels. The sensor is not painful and is in commonly used in neonatal units.

Summary of ethical issues (resolved)

1. The three main ethical issues this study raises are:
   1. that researchers will be asking parents for consent just before or just after the birth of their pre-term baby,
   2. the oximeter readings will be done in peoples’ homes and the pulse oximeter will be blinded, so the family and researchers will not know the readings at the time that they are taken, and
   3. because the meter is recording only (with the alarm switched off) the parents would not know if the baby were to experience sleep apnoea. The researcher explained that the apnoea may happen regardless of whether or not the babies are in the study.
2. The committee noted that the participant information sheet makes reference to the use of caffeine treatment and queried whether this is for parents’ information only. The researcher confirmed that the they will gather data only at this stage and if the data shows that late preterm babies are at higher risk of intermittent hypoxia then it will be used as baseline data for a future randomised controlled trial of caffeine in this group to reduce the risk of intermittent hypoxia.
3. Any respiratory support before study is an exclusion criteria. In the unlikely event that a parent or caregiver gave the baby caffeine themselves, the researchers would keep them in the study regardless.
4. The committee queried whether GPs should be informed but agreed that this is not necessary given the study is an observational study.
5. The researchers will purchase the oximeters.
6. Confidentiality of data – the researcher confirmed that within the research team data will be stored as identifiable to help in further studies (as this is new information which would not be kept in the participants medical records). The data will be de-identified when sharing with other researchers.
7. Home nurses set up pulse oximetry sensors as a standard treatment and will be able to set them up safely in participant’s homes.
8. All preterm babies have checks before they go home so clinicians will be able to pick up whether something abnormal or congenital is occurring. Paediatricians would be notified.
9. The researcher confirmed that they have had some consultation with Maori and Helen Wihongi will also review the protocol. The committee asked that any suggestions that may arise from the consultation be included in the participant information sheet.
10. Please review the information sheet and change wording to reflect that it is written from the perspective of the parent or caregiver. PIS Opening para 3rd sentence, change the last wording to “it won’t affect the care your baby will receive”.

Decision

This application was *approved* by consensus.

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| **3** | **Ethics ref:** | **15/NTA/170** |
|  | Title: | PREVENT Trial |
|  | Principal Investigator: | Dr David Smyth |
|  | Sponsor: |  |
|  | Clock Start Date: | 29 October 2015 |

Dr Doug McClean 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 the study

1. This is a trial of a stent (bioresorbable vascular scaffold, BVS) in heart arteries which have a narrowing which is not limiting the flow of blood through the artery.
2. The primary end point of this study is to test whether the implantation of the BVS scaffold in patients with vulnerable plaque characteristics reduces the incidence of cardiac events (after 2 years) when compared to optimal medical treatment (drug eluting stents). Both groups in the trial will be on statins and both will have standard optimal medical care.
3. The research team will use imaging technology to determine the amount of narrowing that (which would inform inclusion in this study) and looks at the plaque to see whether there are any vulnerable characteristics.

Summary of ethical issues (resolved)

1. The committee queried whether the BVS scaffold is approved for use. The researcher confirmed that it is approved, CE marked and has been available for use since 2013. It is not currently used for arterial narrowing and this is an entirely new trial looking at use in those with vulnerable plaque that can come unstable and cause cardiac events. Standard treatment is currently statins and aspirin.
2. The committee noted that the researchers had stated that there was no sponsor at question a.5.1 on page 9 of the application form. The researcher explained that this is not an industry run trial and is a collaboration – the group is responsible for providing the governance of this study. The committee also noted that question b.4.3 states that restrictions on publication of the data are in place. The collaborative research group is acting as the sponsor and it is appropriate to acknowledge them for that.
3. The committee noted that the researchers had stated at question a.1.6 on page 4 of the application form that there are no ethical issues anticipated and asked whether the research team had had a chance to reflect on whether an experimental implant raised any ethical issues. Although the BVS is approved for flow limiting reasons, there is a risk that it may potentially cause harm, another ethical issue is the timing of gaining participant consent – acknowledging that the patient may be anxious or scared and not knowing what you are going to find is important.
4. Once identified as having vulnerable plaque then patients will be randomised to trial at that time. The researcher explained that being randomised to the trial there and then is typical of these types of trials as patients will be there anyway to receive treatment for flow limiting arteries and this provides an opportunity for their clinicians to identify whether they may be eligible.
5. The researcher confirmed that GPs will be informed and that a letter will be sent to GPs with a copy of the PIS.

The committee requested the following changes to the participant information sheet and consent form:

1. Please include a lay title, review the document and make sure all language is accessible by a lay audience perspective and please remove US spelling.
2. Please include the following ACC statement: “*If you were injured in this study, which is unlikely, you would be eligible* ***to apply*** *for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery.*  
   *If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.”*
3. Please make clear what will happen for the control group in this study. For example, will they receive treatment, will they have extra tests?
4. Please provide more information about the tissue and how it is being used and include a statement that acknowledges that the use and storage of tissue raises cultural issues for some Mãori, how this will be addressed and whether there are any cultural protocols in place for disposal of the tissue.
5. Page 2, ‘Drug-eluting stent implantation (DES)’. The first two paragraphs may be confusing as they may suggest that people with blood-flow limiting narrowings are not eligible for this study. The researchers noted that the inclusion of this information was a sponsor requirement. The committee suggested that the research team include a flow chart or diagram that clearly sets out how you will split patient streams.
6. Please include that an interpreter is available on request at the top of the consent form.
7. Page 5, point 7 ‘Voluntary participation and withdrawal from the trial’: please clarify for participants that safety checks will be in place following any procedure they may have but that they are able to withdraw from further follow up should they wish.

Decision

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

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

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

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| **4** | **Ethics ref:** | **15/NTA/171** |
|  | Title: | EDP 494-001: A study of EDP-494 in healthy subjects and Hepatitis C patients |
|  | Principal Investigator: | Prof Edward Gane |
|  | Sponsor: | Enanta Pharmaceuticals, Inc. |
|  | Clock Start Date: | 29 October 2015 |

Prof Gane and Miss Angelica Bernal 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 the study

1. Given the high prevalence of hepatitis C both globally and within New Zealand and the current high unmet medical need because of high treatment failure rate and tolerability issues with the current standard of care, there is an urgent need to improve and expand therapeutic options for these patients.
2. In order to address this unmet medical need, the design of non-immunosuppressive cyclosporine derivatives have been pursued. This is the first clinical study of EDP-494 to assess the safety, tolerability and pharmokinetics in healthy volunteers and then HCV patients.
3. There is no risk of antiviral resistance and the drug works against all types of hepatitis C. The drug won’t be used as monotherapy.
4. This is a first in human study in healthy volunteers. Participants will start with a single dose, be carefully monitored and if there are no safety issues the dose will be increased in a subsequent cohort. The main safety risks the researchers are anticipating in this study are toxicity effects on bone metabolism. Cortisol thickening has been seen in rats but no other species.

Summary of ethical issues (resolved)

1. The researchers clarified that healthy volunteers will be recruited from the ACS database. ACS has a large database of people who are participating in different studies.
2. The committee queried how many studies, from the researchers’ point of view, participants may enter before their safety becomes a risk. The researchers noted that the GCP requirement is no more than 4 or 5 a year but ACS policy is no more than 2 per year.
3. The researchers confirmed for the committee that the study will be overseen in New Zealand only. Phase II and III studies are typically multi-site studies that are handed over to larger companies.
4. PK samples will be sent to Ohio for testing and destroyed after 5 years. Samples will not be stored in a biobank for future unspecified research.

The committee requested the following changes to the participant information sheet and consent forms:

1. Page 3, point 1.5 ‘Approval by ethics committee’: please removed the statement that the committee may check that the study is running smoothly as the committee is not responsible for this.
2. Page 8, point 5 ‘What would happen if you were injured in the study?’: the committee noted that it is required to check that participants in commercially sponsored trials will be eligible to apply for compensation that is ACC equivalent and noted that the second paragraph on page 8 states that no payment for lost wages will be made from the sponsor. ACC covers lost wages and the committee asks that this statement be removed from the participant information sheet and that the sponsor fulfil its obligation to provide compensation that is ACC equivalent.
3. Page 8: please remove the Mãori tissue statement as it suggests that you are taking samples for future unspecified research, which is not the case.
4. Page 10, second paragraph: the first sentence implies that committee would have access to individual health records and data. The ethics committee does not see this information. Please remove “such as the ethics committee”.
5. Page 11, point 8.2 ‘Why the study might unexpectedly be stopped’: please remove the statement “decisions made in the commercial interests of the sponsor or by local regulatory/health authorities”.
6. Page 8, point 6, ‘What will happen to my test samples?’: the committee noted the statement that PK samples will be sent to a central laboratory called Medpace in Ohio and asked why the samples will be sent overseas when the study is being run in New Zealand. The researchers explained that Medpace is a more advanced laboratory rather than a central laboratory. The committee asked why the samples will be stored for 5 years when no future unspecified research is planned. The researchers were not sure but will find out and clarify for the committee.
7. Section 1.5 Please remove the sentence that states that the committee may check the trial is running smoothly.
8. Page 9: please replace the word “can” with “could” under the heading ‘What bad effects can happen to me by giving these biological samples?’
9. Page 11: the committee asked the researchers to remove the genetic reference. The researchers explained that they now have a test for single polymorphisms and that this does not test genomic or novel information. All collections are done prior to the participants entering the study. The committee asked the researchers to make this clear in the information sheet.

Decision

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

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

This information will be reviewed, and a final decision made on the application, by the Chair and Dr Christine Crooks.

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| **5** | **Ethics ref:** | **15/NTA/172** |
|  | Title: | MINI |
|  | Principal Investigator: | Ms Ying Jin |
|  | Sponsor: | Massey University |
|  | Clock Start Date: | 29 October 2015 |

Dr Louise Brough 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 the Study

1. An observational study involving mother and child, but with no treatment.
2. Measuring iodine, selenium and iron levels in mother and child.
3. Despite national efforts to lift iodine levels, previous surveys of mothers have shown lower than desired levels.

Summary of ethical issues (resolved)

1. The committee congratulated the research team on their response to the ethical issues question a.1.6 on page 5 of the application form.
2. The committee asked whether the researchers will make home visits and was advised that participants will predominantly come to Massey University. If home visits are required the researcher will be accompanied and protocols are in place for the picking up of samples from participants’ homes.
3. The committee asked the researchers to review the information stated under ‘What are the advantages of taking part in the study?’ and be more realistic about how they are presenting the study. For example reference to “how well you and you baby are doing” may be misleading as this study may not give advice about how well they are doing.
4. The committee noted the statement that “Based on your food diary you will receive feedback of your intake of nutrients and this will be compared to New Zealand standard dietary guidelines.” The committee asked how promptly this would occur and the researchers confirmed within a couple of weeks and the committee asked the researchers to state this. The committee asked should people modify their diet as result of any feedback will that affect the data. The researchers stated that it may have some effect but not a huge amount.
5. The committee noted the answer stated at question a.1.5 on page 5 of the application form that the researchers will recruit 200 participants post-partum and a range of ethnicities but did not say what ethnicities they will try and target. The committee recommended that the researchers give further thought about how many women they will recruit into particular groups and come up with a recruitment strategy. The committee asked whether the research team anticipated any problems in getting numbers. The researchers have based their numbers of a sample size population from a previous study. They intend to get people to help out in recruitment.

The committee requested the following changes to the participant information sheet and consent form:

1. The committee thanked the research team for a clear participant information sheet and noted that while the committee encourages succinctness and clarity, it thought that some important details are missing. The committee requested that the researchers add a flowchart to present for mothers (in a stepped out way) what is involved in taking part in this study. i.e that there are visits and what will happen in between the visits.
2. Please include information about how the tissue will be taken, how it will be discarded, how long it will be stored for. For example, the committee asked whether the urine sample taken will be by a cotton ball in the nappy. The researchers confirmed that it will be and the committee asked that they state this in the information sheet.
3. Please include a statement acknowledging that the use and storage of tissue is a cultural issue for some Mãori and that there are cultural protocols in place for the discarding of any tissue. The committee advised that it may be worthwhile for the research team to consult further with Mãori as there are cultural issues around the clipping of nails and how they will be discarded.
4. Please include contact details for the study’s Mãori support person.
5. Please state that data will be held for 10 years after the youngest person in the study has reached the age of consent or 16 years old.
6. Please include a statement advising that if participants change their mind about being in the study that they can withdraw from the study at any time.
7. Consent form: please refer to the HDEC pro forma and include statements that are relevant to your study. It is important to see that participants are clear about what they are consenting to. You can find the HDEC pro forma at: <http://ethics.health.govt.nz/>
8. The research team confirmed that they will tell women about any unusual results and recommend that they see their GPs. Please include this in the participant information sheet.

Decision

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

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

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

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| **6** | **Ethics ref:** | **15/NTA/173** |
|  | Title: | Medical conditions and traumatic brain injury |
|  | Principal Investigator: | Miss Shivanthi Balalla |
|  | Sponsor: | Auckland University of Technology |
|  | Clock Start Date: | 29 October 2015 |

Miss Shivanthi Balalla and Dr Alice Thadom 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.

Ms Kate O’Connor declared a potential conflict of interest and the committee decided that it was not substantial enough to require her to not take part in the discussion or decision-making for this study.

Summary of the study

1. There are two phases to this study: Phase I will look at outcomes in the TBI population and Phase II will compare TBI population with the orthopaedic population using the same data. The researchers will look at pre-medical condition in TBI and orthopaedic and then compare for conditions developed after sustaining an injury.
2. Individuals who have cognitive difficulties will not be eligible to be recruited into this study.

Summary of ethical issues (resolved)

1. The committee asked the researchers to clarify how they intend to recruit participants to this study. The researchers advised that they intend to contact participants identified by the Waikato Hospital Registry who meet eligibility criteria by phone to ask them whether they would like to take part in the study. Consent will be sought from participants for access to their medical information from their hospital records. The researcher would like to have access to 800 records. A low response rate (30%) is anticipated and the researcher will not interview 800 individuals.
2. The committee asked how the researchers intend to get patient names from the Waikato Hospital registry. The researchers stated that they have applied approval from Waikato hospital to release the names and with consent from participants to have access to the medical details relevant to study. No data without consent will be shared and if a person who is contacted declines participation in the study, the information will not be shared beyond the hospital registry. The committee asked the research team to notify the committee when they have a decision from Waikato hospital.
3. The committee asked how the researchers will establish whether a person is being agreeable and is not being coerced into the study. The researchers are conscious of this and will give people the opportunity to ask questions and will check their understanding by getting them to repeat back what is involved. Given that only one researcher intends to do all the interviews, the committee queried whether interviewer fatigue might occur therefore this may not be picked up. The researchers stated that they have allowed a 6-month time frame for interviews and will not conduct them back to back to minimise any risk of fatigue.
4. The committee asked whether the researchers can judge the quality of information participants give and queried whether they will also talk to caregivers. The researchers advised that in most cases participants will be 4 years post-injury and able to talk about their experiences. They will get more authentic information from participants than from their caregivers.
5. The committee noted that it could be stressful for participants if they are told that their TBI contributed to co-morbidities. The researchers advised that they will not offer feedback on an individual level but on a group level. They are looking for associations and trends and they will be careful to report the information sensitively. The committee asked how the researchers plan to manage any questions from participants about whether their TBI has contributed to co-morbidities. The researchers wouldn’t be able to tell and would advise that they are collecting data that does not link to an individual and that they cannot provide clinical advice. The committee asked the researchers to explain this in the participant information sheet introduction.

The committee requested the following changes to the participant information sheet and consent forms:

1. Consent form: – please include yes/no options for the statements that are optional. Pleas remove the ‘no’ option from points numbered 7, 8 and 13.
2. Please make clear upfront that you will not provide advice about whether co-morbidities have affected an individual’s brain injury and vice versa and that when results do come out they will be on a group rather than individual level.

Decision

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

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

This information will be reviewed, and a final decision made on the application, by the Chair and Ms Shamim Chagani.

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| **7** | **Ethics ref:** | **15/NTA/174** |
|  | Title: | Cytisine pharmacokinetics and dose response (C-DRAKS 3 and C-DRAKS 4) |
|  | Principal Investigator: | Miss Soo Hee Jeong |
|  | Sponsor: | University of Auckland |
|  | Clock Start Date: | 29 October 2015 |

Miss Soo Hee Jeong and Dr Malcom Tingle was 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. Smoking is a leading cause of a lost healthy life in New Zealand. Cytisine has been shown to be more effective than placebo in achieving long-term smoking cessation. The researchers have previously conducted two studies on cytisine in humans (single dose study C-DRAKS 1 and multi-dose study C-DRACKS 2) and this study is a continuation of those studies.
2. The researchers explained that the drug has been in use in Europe for 50 years but there is a paucity of pre-clinical data on cytisine. Reports from clinical trials indicate that medication adherence needs to improve and an improved (simpler) dosing regimen may mean people are more likely to take the drug. C-DRAKS 3 and C-DRAKS 4 will be a feasibility study to test this theory.

Summary of ethical issues (resolved)

1. SCOTT review was submitted for C-DRAKS 1 and C-DRAKS 2 and the researchers are not relying on that for this study. They have submitted a further application to SCOTT for this study.
2. This is a dose escalation study. Participants will receive a single dose of cytisine either 1.5mg, 3mg or 4.5mg and participants will be monitored at the clinics to confirm that no adverse events have occurred. No adverse events have been recorded in a previous trial. The researchers will use computer modelling to predict whether they get levels up to satisfactory level to suppress smoking.
3. The researchers are taking a cautious approach and will administer a single dose and if there are no adverse events they will escalate the dose.
4. The researchers are confident that they will be able to get the number of participants needed for this study (48). Recruitment will be via advertisements at and outside of the university and participants will be reimbursed for their time.
5. The researchers confirmed that there will be support for people who want to quit smoking in place.
6. The researchers confirmed that the study drug is extracted from a plant but is formulated in the lab where there are quality control processes in place to ensure that the concentration is consistent.
7. The researchers confirmed that Pfizer is not sponsoring this study. This study is being run out of the centre of addiction research at the university a policy of not accepting money from tabacco companies is in place. There are no manufacturer restrictions on publication of results.
8. A questionnaire on Cultural acceptability that asked whether Maori would be more or less likely to use the drug made from the Kowhai compound found that people would be more likely to use it. The researchers explained that prior research carried out through a public health policy team has found that cytisine would be acceptable to be packaged as “Rongoã Mãori” as a plant compound from the Kowhai tree makes the same compound.
9. The researchers confirmed that consultation with Maori has been done and the committee asked that the researchers provide the committee with the letter showing this and also if any changes were suggested as a result that they be made.
10. The committee noted one of the inclusion criteria that participants must smoke at least 10 cigarettes a day aligning the inclusion criteria with large smoking cessation trials. The researchers advised that smokers are used to nicotine and the use of this product should make no difference.

The committee requested the following changes to the participant information sheet and consent form:

1. Please replace the current compensation clause on page 3 with the following statement: insert: *If you were injured in this study, which is unlikely, you would be eligible* ***to apply*** *for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery.  
     
   If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.*
2. Please update the approving committee to the Northern A Health and Disability Ethics Committee.
3. 10-11 hours is a long day for a smoker without a cigarette. Make clear that they cannot do this and they can walk off campus.

Decision

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

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| **8** | **Ethics ref:** | **15/NTA/175** |
|  | Title: | The “rectosigmoid brake” as a neuromodulation target for faecal incontinence |
|  | Principal Investigator: | Associate Professor Ian Bissett |
|  | Sponsor: | University of Auckland |
|  | Clock Start Date: | 29 October 2015 |

Dr Anthony Lin was 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 the study

1. Sacral neuromodulation is a new technology used for people with faecal incontinence and is becoming the preferred treatment. Earlier research has shown sacral neuromodulation may increase sphincter tone and rectal sensitivity, but little is known about how it works/what the mechanism is.
2. A new technology called high resolution colon manometry will allow the research team to examine pressure waves in the rectosigmoid region centimetre by centimetre. The research team will analyse the manometry images and record what is happening for 24 hours after the sacral nerve stimulator is used. Sacral neuromodulation is standard treatment.

Summary of ethical issued (resolved)

1. The committee noted that the research team has set a specific number of calories for meals and asked whether research team will assess participants prior to the study to know what their normal meal calorific intake is. The research explained that the manometry measures colon movement and that 700 calories is the standard number of calories to stimulate the colon after a meal.
2. The committee asked whether there is any risk of bleeding after removal of the catheter. The researcher confirmed that there is but it is a small risk. Gentle traction is applied when removing and this won’t cause damage. Patients will stay for an hour after removal to give enough time to observe whether there will be any symptoms that need investigating.
3. The research team do not foresee any ethical issues. They are not selecting patients, nor keeping them in hospital for longer. Patients stay overnight so this provides a good opportunity for the research team to do this study.
4. The researcher confirmed the consent process for this study. The participants’ treating doctor is their study doctor. Clinicians hold a regular pelvic floor conference where they discuss cases of patients with issues. If it is thought that a patient is eligible to enter the study, the colorectal nurses will approach them and ask if they wish to be involved in this study. If they agree, then a member of the research team will contact them.
5. The committee asked why the researchers have included a question about level of education for potential participants. The researcher advised that they are using a standard questionnaire for people who would normally come in for sacral stimulation therapy. Knowing socio economic status in the general population could be useful data to show how common this condition is in different groups.

The committee requested the following change to the participant information sheet and consent form:

1. Page 5: please change name of the approving ethics committee to the Northern A Health and Disability Ethics Committee.

Decision

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

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| **9** | **Ethics ref:** | **15/NTA/176** |
|  | Title: | Radiotherapy or Imiquimod in treatment of complex lentigo maligna |
|  | Principal Investigator: | Mr Richard C W Martin |
|  | Sponsor: | Australia and New Zealand Melanoma Trials Group |
|  | Clock Start Date: | 29 October 2015 |

Mrs Gill Rolfe and Mr Richard Martin 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.

Dr Christine Crooks declared a potential conflict of interest, and the Committee decided that she would not take part in the discussion or decision-making for this application.

Summary of study

1. The purpose of this study is to investigate the effectiveness of using either radiotherapy or Imiquimod to treat lentigo maligna, when surgery is not possible or is refused by the individual. Sometimes surgery may not be feasible due to the site of the lesion as these are often found on the face, head and neck and complete surgical excision may not be possible and may be disfiguring.
2. Lentigo maligna is a superficial in situ melanoma which will progress to invasive melanoma. For lentigo maligna that is inoperable the standard of care is radiotherapy. This study will look at whether the use of Imiquimod is more effective than radio therapy in treating lentigo maligna.

Summary of ethical issues (resolved)

1. The committee queried whether Imiquimod is approved for use in New Zealand for treatment of other conditions. The researcher confirmed that it is and is used for the treatment genital warts and basal cell carcinoma. There is sufficient evidence about the cream to know the appropriate dose and efficacy in other indications is well-documented.
2. SCOTT have advised that approval is not needed for use in a different population.
3. When Maori consultation has occurred please provide a letter to the ethics committee.
4. The committee noted that the application states that photographs will be taken. There is a requirement to have a photo taken prior to and after treatment. A secondary endpoint of this study is to do with scarring. The research team will give patients questionnaires to get their perception of scarring and the questionnaires and photos will also be assessed by the clinical team. Any participant will be given a study number and one person will hold the log - any information shared will be purely with a participant’s information number.
5. The committee noted that some people may not wish to have radiotherapy and asked how the research team will manage expectations. The researchers advised that if patients choose to take part in the trial the research team will explain that they have a 50/50 chance of being assigned to cream arm or the radiotherapy arm. Participants will know what treatment they are getting at the outset of the study.
6. A collaborative research group is responsible for the management of the study and the group is not a commercial enterprise. The commercial maker is not funding the study but the committee noted that a commercial insurance certificate was included with the application. The researcher confirmed that the Australian part of the research group is securing funding for study associated costs. The committee advised that for non-commercial research the ACC compensation provisions apply and while commercial insurance is nice to have, it is unnecessary in NZ. The clause on page 8 of the participant information sheet may be a legacy from the Australian group. The committee asked that the research team replace the compensation statement on page 8 with the following: *If you were injured in this study, which is unlikely, you would be eligible* ***to apply*** *for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery. If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.*

The committee requested the following changes to the participant information sheet and consent form:

1. The committee asked that the research team replace the compensation statement on page 8 with the following: *If you were injured in this study, which is unlikely, you would be eligible* ***to apply*** *for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery. If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.*
2. Please review the document for Australian references and replace them so that they are relevant to a New Zealand audience.
3. Please state what will happen to the biopsy samples and how long they will be stored for.
4. Please update the approving committee to the Northern A Health and Disability Ethics Committee.
5. Please include the following from the HDEC PIS/CF pro-forma:
   * If you want to talk to someone who isn’t involved with the study, you can contact an independent health and disability advocate on:
     1. Phone: 0800 555 050  
        Fax: 0800 2 SUPPORT (0800 2787 7678)  
        Email: [advocacy@hdc.org.nz](mailto:advocacy@hdc.org.nz)

* For Maori health support please contact :
  + 1. *Name, position*

*Telephone number*

*Email*

* You can also contact the health and disability ethics committee (HDEC) that approved this study on:
  + 1. Phone: 0800 4 ETHICS
    2. Email: hdecs@moh.govt.nz

1. Please review the document for typos.
2. Page 8, point 13: makes reference to ethics committees having access to health information. Please remove this as HDECs do not have access to an individual’s health information.
3. Consent form: as GPs will be informed about participation in this study. Please include this statement in the consent form.
4. Withdrawal of participation does not have to be in writing. Participants just have to notify their study doctor. Please make sure that this is optional in the consent form.

Decision

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

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

This information will be reviewed, and a final decision made on the application, by the Chair and Ms Susan Buckland.

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| **10** | **Ethics ref:** | **15/NTA/183** |
|  | Title: | The IMPERIAL Study |
|  | Principal Investigator: | Dr Andrew Holden |
|  | Sponsor: | Boston Scientific Pty. Ltd. |
|  | Clock Start Date: | 29 October 2015 |

Mrs Donna Katae and Dr Holden 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 the study

1. This stent (Eluvia) was tested in a first in man trial (MAJESTIC trial) and at 12 months results showed it met its effectiveness endpoint at around 97 percent. The study device has been used before with no safety concerns. The researchers want to show non-inferiority with products on the market. The condition being treated is peripheral artery disease.
2. This study will randomise the device against current treatment and it is anticipated that the trial will be multi-centre and include 57 patients across New Zealand and Australia.
3. The trial will evaluate the safety and effectiveness of this Boston Scientific device.

Ethical issues (resolved)

1. The committee accepted the design and technical capabilities of the device itself and noted that the trial is well designed. The committee was satisfied that follow up is all standard of care, elongating follow up is to be applauded and patients don’t have anything invasive.
2. Dr Holden explained that previous stent trials were compared to balloon angioplasty (as gold standard).
3. However, it is important to also know how one device compares to another. In this case the research team will be comparing the current commercially available Zilver PTX as the control and in evaluating the effectiveness and safety of the Eluvia stent. The Eluvia is well tested (latest, the Majestic trial) whereas the Zilver PTX is the only stent approved for use in the SFA proximal popliteal artery
4. The committee noted that the FDA had approved the IDE application as a staged study, which is interpreted to mean that the sponsor could only expand the study after it had submitted an IDE supplement responding to FDA concerns on nominated deficiencies. As the FDA approval is limited to 75 US institutions and 100 subjects, and the proposal calls for 485 participants in several countries, could the researcher please clarify if the NZ testing will start before the US, or will the US start first and address the deficiencies as noted by the FDA.

Ethical issues (outstanding):

1. The committee queried the FDA limitation that the study has been approved with a site waiver as a staged study and can proceed in 75 US institutions and 100 US patients. The researchers explained that they had spoken with the sponsor about this and asked for a response to the FDA concerns. The sponsor wished to proceed with an ethics application in New Zealand regardless.
2. The committee queried the make-up of the data safety monitoring committee and noted the requirement for it to have membership limited to individuals free of any significant conflict of interest in relation to the study being monitored, whether financial, intellectual, professional or regulatory in nature. The committee would like to know the make-up of the DMC and whether it is considered to be independent.

The committee requested the following changes to the participant information sheet and consent form:

1. Page 6, ‘Confidentiality’: please include that when participants exit the study their personal information collected prior will continue to be used for presentations.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Please provide membership details for the data monitoring committee and whether you consider the committee to be independent of those conducting the study (*Ethical Guidelines for Intervention Studies* *para 6.55*).
* Please provide a response from the sponsor to the FDA limitations set out in the letter of scientific review submitted with this application. (*Ethical Guidelines for Intervention Appendix 1*)

This information will be reviewed, and a final decision made on the application, by the Chair and Dr Christine Crooks.

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| **11** | **Ethics ref:** | **15/NTA/184** |
|  | Title: | LJPC-501 in Patients with Catecholamine-Resistant Hypotension |
|  | Principal Investigator: | Dr Paul Young |
|  | Sponsor: | La Jolla Pharmaceutical Company |
|  | Clock Start Date: | 29 October 2015 |

Dr Paul Young, Dr Gary Mulholland and Stephanie Pollard 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 the study

1. A common problem in ICU is low blood pressure after a life threatening problem. Either the heart is not pumping adequately and or a person’s blood vessels are too relaxed. It often occurs after a severe infection and is common.
2. The current standard of care is to use catecholamines to restrict vessels, however, 5-7 percent of people are resistant to this treatment and their blood pressure remains critically low. When that occurs clinicians try other therapies and they can work to variable degrees. These patients are at high risk of developing multi organ failure and death. In this study the research team will to randomise patients to two arms: arm one is placebo, which is best possible standard care and arm two is best possible standard care and the study medication, Angiotensin II. The study hypothesis is that Angiotensin II will increase blood pressure.
3. The researcher reiterated that all patients will get best care and the protocol mandates more care than they would usually receive.
4. Angiotensin II is approved by the FDA for licencing purposes.

Summary of ethical issues (resolved)

1. The main ethical issue in this study is that participants will generally not be able to provided informed consent prior to participation in the study because of the severity of their illness. Patients will all receive standard of care and if the standard of care is not effective they will be randomised to potentially receive the study treatment.
2. The researchers will not take blood for future unspecified interest as they accept that they cannot show that use would be in the best interests of the participant.
3. The vast majority of participants cannot consent prospectively as they are too unwell. When treating clinicians think that enrolling in the study is in a person’s best interests to do so they will ask family members for their opinion but not for their proxy consent. The enrolment window is wide and the expectation is that the standard approach will be to sit down with family and discuss pros and cons and assess wishes and if they think that the participant would want to take part then they will enrol them in the study. As soon as the participant is competent the research team will ask for prospective consent and continued participation.
4. The committee was satisfied that in a life-threatening situation that participants will receive the best available treatment and that the researchers will, when possible, try to get consent from the person beforehand while acknowledging that the proportion of patients who will be competent to consent will be low.
5. If prior consent is not possible, the researchers will get consent after patient recovery. If the patient chooses not to consent and or does not think that their family member/s opinion that taking part would have been consistent with their wishes then the researchers will withdraw them from the study.
6. In the event that the patient recovers and does not consent to the use of their data and any more medication treatment related to this study they can decline. The research team would like to continue to collect data for safety reasons. The committee agreed to this.
7. The committee was satisfied that the research would be in the best interests of the participants.

The committee requested the following changes to the participant information sheet and consent form:

1. The committee complimented the research team on the way the participant information sheet is written and on the three options offered in the form.
2. Page 2: please reword paragraph 7 to make clear that participants will be randomised to receive standard of care with placebo or study medication with standard of care.
3. Page 5, ‘What if something goes wrong?’: the committee noted that in New Zealand, participants in commercially sponsored trials should be compensated to the same extent as ACC. Please remove the second and third paragraphs as the sponsor cannot put qualifications on what is provided so that it is not equivalent to ACC compensation. Should there be a dispute it must be resolved between the sponsor and the participant not between the participant and the sponsor’s insurer.
4. Page 7, ‘What happens after the study or if I change my mind?’: please state where you will send the sample, how long it will be stored, and how it will be discarded.
5. Consent form: please include a ‘yes/no’ option for points 7 and 8. Please remove the ‘no’ option from the other points.

Decision

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

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

This information will be reviewed, and a final decision made on the application, by the Chair and Miss Shamim Chagani.

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| **12** | **Ethics ref:** | **15/NTA/185** |
|  | Title: | Management of Refractory Cancer Ascites (MORCA) |
|  | Principal Investigator: | Dr Celia Palmer |
|  | Sponsor: |  |
|  | Clock Start Date: | 29 October 2015 |

Dr Celia Palmer was present in person for discussion of this application.

Potential conflicts of interest

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

Dr Christine Crooks declared a potential conflict of interest, and the Committee decided that Dr Crooks would not take part in the discussion or decision-making for this application.

Summary of the study

1. This study will look at the best method of managing malignancy related ascites when chemotherapy can no longer be offered. The current management involves having fluid drained regularly via a needle by a doctor.
2. The researchers want to find out if an indwelling catheter placed under the skin, so that fluid can be drained at home, would be safe and benefit the patient’s quality of life.

Summary of ethical issues (resolved)

1. The committee asked who is responsible for the initiation, management, and financing arrangements of the study. The DHB is the sponsor.
2. The committee noted the answer given at question p.4.3.1 on page 22 of the application form. The researcher confirmed that she has consulted with Helen Wihongi.
3. The committee noted the answer given at question r.2.5 on page 17 of the application form that health information will be stored for three years and reminded the research team of the legal obligation to store for a period of 10 years.
4. The committee asked whether the researchers expect any more SAES with an indwelling catheter. The researcher noted that they did not know and that this is why they are doing the study. They have the right support in place for the ‘home’ arm of the study.

The committee requested the following changes to the participant information sheet and consent form:

1. Please review the document and remove US spelling so that it is relevant to a New Zealand audience.
2. Please update that ethical approval is from the Northern A Health and Disability Ethics committee.
3. Please include the following compensation clause: *If you were injured in this study, which is unlikely, you would be eligible* ***to apply*** *for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery. If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.*
4. Please include the following from the HDEC PIS/CF pro-forma:

If you want to talk to someone who isn’t involved with the study, you can contact an independent health and disability advocate on:

* + 1. Phone: 0800 555 050  
       Fax: 0800 2 SUPPORT (0800 2787 7678)  
       Email: [advocacy@hdc.org.nz](mailto:advocacy@hdc.org.nz)

For Maori health support please contact :

* + 1. *Name, position*

*Telephone number*

*Email*

You can also contact the health and disability ethics committee (HDEC) that approved this study on:

* + 1. Phone: 0800 4 ETHICS
    2. Email: hdecs@moh.govt.nz

1. Following up with a weekly visit with the patients. Not true for people on the treatment care arm. Please distinguish that.
2. Please update the Maori contact person with Helen Wihongi’s details.
3. Consent form: please review the statements on the consent form and think about what are truly yes/no options. Please remove the ‘no’ option for statements that are not options.

Decision

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

## 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:** | 01 December 2015, 08:00 AM |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

The meeting closed at 6.30pm