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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 11 November 2014 |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

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| **Time** | **Item of business** |
| 1.00pm | Welcome |
| 1.10pm | Confirmation of minutes of meeting of 07 October 2014 |
| 1.30pm | New applications (see over for details) |
|  | i 14/NTA/179  ii 14/NTA/180  iii 14/NTA/181  iv 14/NTA/183  v 14/NTA/186  vi 14/NTA/187  vii 14/NTA/194  viii 14/NTA/185  ix 14/NTA/190  x 14/NTA/191  xi 14/NTA/192  xii 14/NTA/193 |
| 6.15pm | General business:   * Noting section of agenda |
| 6.20pm | 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 |
| Ms Shamim Chagani | Non-lay (health/disability service provision) | 01/07/2012 | 01/07/2015 | Present |
| Mr Kerry Hiini | Lay (consumer/community perspectives) | 01/07/2012 | 01/07/2015 | Present |
| Ms Michele Stanton | Lay (the law) | 01/07/2012 | 01/07/2015 | Present |
| Dr Karen Bartholomew | Non-lay (intervention studies) | 01/07/2013 | 01/07/2016 | Present |
| 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 | Present |

## Welcome

The Chair opened the meeting at 1.11pm and welcomed Committee members, noting that no apologies had been received.

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 7 October 2014 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **14/NTA/179** |
|  | Title: | 7 Day AHED Study |
|  | Principal Investigator: | Dr Paul James Quigley |
|  | Sponsor: | Australasian College For Emergency Medicine |
|  | Clock Start Date: | 30 October 2014 |

Dr Paul Quigley was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of ethical issues

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

* The Committee commended the researcher for a well put together application, which was a worthwhile and important study.
* Dr Quigley explained that this study will be done in Australia and at Wellington Hospital and Hawke’s Bay Regional Hospital for seven days with the aim of establishing the burden of health harms from alcohol, ranging from obvious injuries to psychological harm and chronic illness.
* Dr Quigley explained that they will also be asking if alcohol is a secondary cause of their presentation at the ED, for example if a person is homeless and this is due to alcohol.
* Dr Quigley explained that this study is a standardised approach with each ED asking the same pre-screening and formal screening questions to establish harm. This will enable researchers to get a cost of the burden of alcohol at a macro level and individual level in Australasia. He said they will be screening all presentations to ED for alcohol, while at present the screening is currently limited to mental health patients and those presenting with injuries.
* The Committee asked for an explanation of the consent process. Dr Quigley explained that the standard care is to ask four initial screening questions to determine whether an ED presentation is due to alcohol. If a patient is deemed to be alcohol positive, they will go through the consent process for having data collected. Participants aged 14 and 15 will require written consent by a parent or guardian, while 16 and 17 year olds will require verbal consent from a parent or guardian. Dr Quigley acknowledged that consent cannot be obtained from an intoxicated patient so the consent may need to be obtained prior to discharge or with a follow up phone call.
* The Committee asked how clinically intoxicated people would have to be before they cannot participate. Dr Quigley explained that there is a scale based on appearance and behaviour, for example being able to walk in a straight line or reading text. If people appear able to retain information and have no physical signs of intoxication, they would be regarded as sober. There is also the ability to use a breathalyser, with most literature saying that a person with alcohol levels no higher than 80mg can provide consent.
* The Committee asked how the questionnaire would work, particularly for children. Dr Quigley advised that it is a facilitated interview with a screener, who has been trained in counselling, present. If the screener feels that a child is not fully divulging everything as a parent is in the room, they will ask to do the interview in a separate room.
* The Committee advised that information needs to be stored for 10 years from when the youngest participant turns 16.
* The Committee advised that it would be preferable to allow 16 and 17 year olds to consent for themselves as this fits in with the Care of Children Act which allows for people younger than 18 to give consent.
* The Committee asked if the demographic information listed on page 13 of protocol would only be collected for alcohol positive patients. Dr Quigley advised that this data would be collected for all patients. The Committee advised that there would need to be signs in the ED informing patients that they will have additional information collected. The Committee asked to see a copy of the wording of the signs.
* The Committee noted that the PIS states that an AUDIT score of 16 may be shared but the application talks about 20. Dr Quigley explained that for scores of 16 to 20, they would want to discuss with participants and ask to pass on to their GPs. He said that a score of 20 or above is considered truly hazardous and participants would need to have discussions with the community alcohol and drug group about ongoing counselling.
* The Committee advised that ethnicity data needs to be collected using the standard Ministry of Health collection methods.
* The Committee noted that incompetent or terminally ill people would be excluded from the study but that there was no criteria listed for defining these groups.
* The Committee requested the following changes to the Participant Information Sheet and Consent Form:
  + Please amend PIS from one centre in New Zealand to two (page 2 of the PIS).
  + Please include an ACC compensation clause. Suggested text can be found on the PIS template at <http://ethics.health.govt.nz/>.
  + Please include that this study has received ethical approval from the Northern A Health and Disability Ethics Committee.
  + Please add New Zealand contact details, including HDC advocacy and Māori cultural support.
  + Please include that AUDIT scores higher than 16 may be given to participant’s GPs and that those with scores of more than 20 will be referred to the community and alcohol drug team.
  + Please provide New Zealand equivalents for all Australian references in the PIS.
  + Please include if follow up data will be collected in the PIS.

Decision

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

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

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| **2** | **Ethics ref:** | **14/NTA/180** |
|  | Title: | Pulse oximeter and arterial oxygen saturation recordings in Intensive Care Unit patients. |
|  | Principal Investigator: | Dr Janine Pilcher |
|  | Sponsor: |  |
|  | Clock Start Date: | 28 October 2014 |

No researchers were present for discussion of this application.

Potential conflicts of interest

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

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

Summary of ethical issues

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

* The Committee noted that this was an observational study comparing two measures of oxygen concentration levels, either an arterial blood gas sample (ABG) or pulse oximetry. The study will compare measurements between 200 patients in an ICU setting in New Zealand. As the study will be done in an ICU, patients will not be well enough to provide consent. The committee noted this was measurement only and not treatment.
* The Committee asked for clarification on the rationale behind the study and noted that their understanding was that the idea was to reduce the amount of ABGs done and rely more on pulse oximetry as it is non-invasive.
* The Committee noted that this was a relatively low risk study, with the risks being around information and privacy. They advised that a participant information sheet needs to be provided, giving participants the option to withdraw access to their data when they recover.
* The Committee queried whether the amount of time taken to monitor the measures would be an appropriate use of ICU staffs’ time. They asked that a letter of support be provided from the General Manager or Head of ICU at CCDHB confirming their willingness to take part in this study.
* The Committee were concerned that the peer review was not independent given that this study was being done on ICU patients. They asked that a peer review independent of MRINZ or the named study investigators be provided.
* The Committee asked for confirmation on who is funding the study (R.5.1).
* The Committee advised that if researchers were collecting NHIs that data would not be de-identified (R.2.4.1).

Decision

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

* Please provide a participant information sheet and consent form *(Ethical Guidelines for Observational Studies, para 6.10).*
* Please provide independent evidence of scientific review *(Ethical Guidelines for Observational Studies, para 5.8).*

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

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| **3** | **Ethics ref:** | **14/NTA/181** |
|  | Title: | Nicotinamide for bronchiectasis |
|  | Principal Investigator: | Dr Conroy Wong |
|  | Sponsor: | CCRep |
|  | Clock Start Date: | 30 October 2014 |

Dr Conroy Wong was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of ethical issues

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

* The Committee asked for the researcher’s thoughts on the safety of nicotinamide at such high doses. Dr Wong explained that nicotinamide was recently described as having anti-bacterial properties. This study will look at the anti-bacterial and anti-inflammatory benefits in people with bronchiecstasis.
* Dr Conroy explained that he had done a pilot study of eight patients and this study has been designed based on its findings. He said that the pilot study was a dose escalation study starting from 3g daily, then moving to 4g daily, 5g daily and 6g daily. Dr Wong explained that previous data in diabetes patients showed that people can tolerate 3g daily for up to five years with no difference between the placebo and active drug. In the pilot study Dr Wong reported nausea was the most common side effect with doses above 4g per day. One participant experienced a serious adverse event and was hospitalised with severe nausea, elevated liver function test and mild neutrophilia. The participant recovered following discontinuation and LFT levels returned to normal within a week.
* Dr Conroy explained that this study would look at lower doses and believed 4g would probably be the tolerable clinical limit. Participants will start with a dose of 3 g a day for a week, followed by 3.5g day for a week then 4 g a day for six weeks.
* The Committee asked for clarification on the effect of nicotinamide on neutrophil levels noting neutrophilia can be associated with systemic inflammation. Dr Wong explained that neutrophils also defend against bacterial infection. Apart from the serious adverse event noted in the pilot study nicotinamide had been shown to cause mild neutrophilia. He advised that the researchers will be closely monitoring neutrophil counts in blood tests.
* The Committee noted that this was a Phase II study primarily investigating safety and efficacy and asked if a long term study was planned. Dr Wong advised that if this study finds the efficacy endpoints and the drug is tolerable, then he would consider a large, randomised, controlled trial.
* The Committee noted that the HRC had advised that an independent data monitoring committee was not necessary and asked if the researchers had considered including another independent member in their DMC given that they were still investigating efficacy issues. Dr Wong advised that another person could be added but that he did not know if this would add any value to the committee. He advised that the committee consisted of two clinicians and one biostatistician. The Committee asked if an immunologist would be considered if another member was added. Dr Wong advised that given that the problems would be toxicity from liver function test abnormalities, nausea and an increase in neutrophil levels, the issue would be who would stop the study, so the committee would need people who could make decisions around that.
* The Committee asked where participants would be recruited from. Dr Wong advised they would be from Middlemore Hospital, patients enrolled previously in bronchiectasis studies and from discharge record coding.
* The Committee advised that researchers should take account of any issues raised in the Māori consultation and add to the PIS if necessary.
* The Committee requested the following changes to the Participant Information Sheet and Consent Form:
  + Please move the paragraph on the purpose of the study to the opening paragraph of the PIS to make it more understandable to the participant.
  + Please review the first two paragraphs of the PIS for repetition.
  + Please be consistent on whether participants can withdraw the use of their data (pages 5 and 6 of the PIS).
  + Please remove the sentence “this consent does not have an expiration date”.
  + Please amend Injury Prevention, Rehabilitation and Compensation Act to the Accident Compensation Act 2001 (page 6 of the PIS).

Decision

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

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

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| **4** | **Ethics ref:** | **14/NTA/183** |
|  | Title: | Neonatal and Infant Eye Screening in New Zealand |
|  | Principal Investigator: | Dr Shuan Dai |
|  | Sponsor: | The University of Auckland |
|  | Clock Start Date: | 30 October 2014 |

Dr Shuan Dai and Ms Samantha Watkins were present in person for discussion of this application.

Potential conflicts of interest

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

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

Summary of ethical issues

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

* The Committee noted that there was some confusion about the different elements of the study and asked for an explanation from the researchers. Ms Watkins explained that there are three main aspects to the study. She said that the RetCam had been used in Auckland for about seven years in premature babies who are at risk of retinopathy of prematurity (ROP). The researchers now want to review this programme in a real world setting and children who have had ROP will come for a full eye test to review the long term outcomes. Children without ROP will also be tested using the SVOP machine. Ms Watkins said there are some concerns around eye testing as a lot children are presenting late with congenital cataracts or retinoblastoma and the third part of the study will be testing newborns using the RetCam.
* Ms Watkins advised that her PhD will be based on the effectiveness of screening but a full answer cannot be given without looking at long term data. She said that she will be coordinating the project and doing the consent process, a trained team of a medical photographer and nurses will take images with RetCam and Dr Dai will analyse the images.
* The Committee advised that as there are three elements to the study (universal newborn screening, follow up of children with ROP and SVOP machine testing of children who have not had ROP), separate PIS should be provided as different information is required. The PIS need to be written from the perspective of parents reading it, for example “your child”.
* The Committee advised that particular care needs to be taken around universal screening for newborns as there are different ethical issues than for testing on premature babies, where extra testing would be expected.
* Ms Watkins advised that this project had been discussed with Associate Professor Papaarangi Reid and had been altered based on her comments. The Committee recommended discussing the study with Dr Helen Wihongi at Auckland DHB, with particular attention to the newborn screening project and reducing inequalities.
* The Committee noted that the protocol had discussed non-accidental injuries (NAI) for retinal haemorrhaging and recommended exercising care to avoid stigmatisation given that retinal haemorrhages can occur during birth, and that previous studies had suggested that haemorrhages may be common (10-20% births) and the natural history was not well understood. The Committee recommended including a lay commentary outlining these points in the PIS, and also suggested discussing the issue of potential stigmatisation with Dr Wihongi.
* The Committee asked whether the sample size of 500 newborns (in addition to the 200+ children for the ROP arm) would be achievable in the context of a PhD. Ms Watkins believed so as there are 7,500 children born at Auckland Hospital each year. She has had discussions with Dr Malcolm Battin who is in charge of NICU and will contact private providers so that the study can be discussed with parents before the birth. The six week return visit is only required for those children with retinal haemorrhages.
* The Committee requested the following changes to the Participant Information Sheet and Consent Form:
  + Separate PISCF for the different arms of the study, written from the perspective of the parents/caregiver of the infant/child.
  + More detail, in lay language, on exactly what will happen to the infants/children in each arm of the study if they agree to participate.
  + Please include an introductory statement in the PIS that this is PhD project for Ms Watkins.
  + Please include names for the contact details.
  + Please include more information on the eye drops.
  + Please include details of project funding.
  + Review the withdrawal statements in the PIS text and CF (currently one indicates the ability to withdraw data and the other does not).

Decision

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

* Please provide three separate participant information sheets *(Ethical Guidelines for Observational Studies, para 6.10).*
* Please amend the participant information and consent form, taking into account the suggestions 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 Ms Shamim Chagani and Ms Susan Buckland.

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| **5** | **Ethics ref:** | **14/NTA/185** |
|  | Title: | EPED |
|  | Principal Investigator: | Associate Professor Andrew Holden |
|  | Sponsor: | EMBA Medical, Inc. |
|  | Clock Start Date: | 30 October 2014 |

Associate Professor Andrew Holden and Ms Helen Knight were present in person for discussion of this application.

Potential conflicts of interest

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

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

Summary of ethical issues

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

* The committee noted this was First-in-Human trial.
* When questioned about the last 20 or so trials the team has carried or are underway, Dr Holden replied that 14 were FIH.
* A/Prof Holden explained that coils or plugs are generally used to block an artery. The EPED device is similar to a plug and will compete with current technology. He explained that with current plugs, it is difficult to know if the artery is properly blocked as it usually takes about an hour or two to block an artery. The study device will be used in indications which currently use plugs. The device will use guidewires to deploy the blocking material, in a similar way to current stent techniques.
* A/Prof Holden explained that there have been some cases (using current treatment) where the blood is still flowing after it is thought it had been blocked. He said he had looked at the literature and devices can be given approval even without knowing if the artery has been properly blocked. He said that this study has been designed with follow up to ensure that the artery has been blocked as an outcome.
* The Committee asked for clarification on the DSMB. Ms Knight advised that there is an independent clinical events committee, with a physician assessing the safety data as it becomes available. The Committee asked if there could be anyone from New Zealand included. A/Prof Holden agreed to ask if a local physician could be involved.
* The Committee noted that the peer review had been provided by the sponsor and was therefore not independent. A/Prof Holden advised that it was difficult to get anyone with the knowledge in New Zealand to provide peer review. The Committee asked if anyone was available internationally. A/Prof Holden agreed that he could ask colleagues, but that this would come with a cost. He said that the ideal situation would to have a specialist peer review committee funded by HDEC to provide independent peer review. The Committee agreed to discuss options for peer review with the HDEC Secretariat.
* Please amend “insurers” to “sponsors” (page 5 of the PIS) and add the clause about investigators not following the protocol.

Decision

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

* Please amend the participant information and consent form, taking into account the suggestions by the Committee *(Ethical Guidelines for Intervention Studies, para 6.22).*
* Please discuss with the sponsors whether an independent peer review can be provided *(Ethical Guidelines for Intervention Studies, para 5.11).*

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| **6** | **Ethics ref:** | **14/NTA/186** |
|  | Title: | Thymine test for 5-FU side effects |
|  | Principal Investigator: | Dr Nuala Helsby |
|  | Sponsor: | The University of Auckland |
|  | Clock Start Date: | 30 October 2014 |

Dr Nuala Helsby 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 she would not take part in the discussions and voting.

Summary of ethical issues

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

* Dr Helsby explained that 5-FU is a key anti-cancer therapy in certain types of cancer, however it is associated with quite severe toxic side effects which can be sudden and life threatening. This is thought to be due to an inherited liver enzyme deficiency but this deficiency does not account for all people at risk of serious side effects.
* Potential participants in this study will be those coming into the clinic about to start treatment with 5-FU. They will be given thymine to see whether they can metabolise it as 5-FU is processed in the same way as thymine.
* The Committee commended the researcher for an excellent and clear PIS, application and protocol.
* The Committee advised that the optional biobanking explained on page 2 of the PIS should be included under a separate heading (like the PK optional substudy is) to make it clear that this part is optional.
* For the section on biobanking, the Committee recommended referring to the Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes at http://www.health.govt.nz/publication/guidelines-use-human-tissue-future-unspecified-research-purposes-0. They asked that information be provided on whether any samples will be sent overseas at a later date, the length of time that samples will be stored, whether people can have samples destroyed if they withdraw or if next of kin asks for them back and information on intellectual property.
* The Committee asked whether participants would be informed of clinically significant results for incidental findings. Dr Helsby advised that they had discussed within the team, and were still debating whether potential (although unlikely) IFs would be returned. On reflection Dr Helsby replied that they would not be testing for anything unrelated to the study so there would be no incidental findings to inform participants of. The PIS will need to be amended to reflect this.
* Dr Helsby advised that Māori consultation is being done through Auckland DHB.
* The Committee noted that if looking at genes, the New Zealand Census ancestry question for genomics needs to be used.
* The Committee requested the following changes to the Participant Information Sheet and Consent Form:
  + Please remove the yes / no options on the consent form for all but the truly optional statements.
  + Please include the PK sub-study on the consent form.
  + Please consider the wording around the optional consent to ensure that participants understand what they are consenting to for future unspecified research.

Decision

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

* Please amend the participant information and consent form, taking into account the suggestions by the Committee *(Ethical Guidelines for Observational Studies, para 6.10).*

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| **7** | **Ethics ref:** | **14/NTA/187** |
|  | Title: | REDUAL-PCI |
|  | Principal Investigator: | Dr Chris Nunn |
|  | Sponsor: | Boehringer Ingelheim Pty Limited |
|  | Clock Start Date: | 30 October 2014 |

Mrs Liz Low and Ms Rachael Monkley were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of ethical issues

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

* Mrs Low explained that this was a study comparing two anti-thrombotic therapies for patients with arterial fibrillation who have had a Percutaneous Coronary Intervention (PCI) procedure. As these patients are at risk of stroke, they need to take anticoagulants (either warfarin or dabigratran) and anti-thrombotic treatment to prevent clotting in the first six to twelve months after surgery (clopidogrel or ticagrelor). Those on warfarin also need to take aspirin. This trial is being run by the makers of dabigatran.
* Mrs Low explained that the aim of this study is to find which treatment regimen is safer and more effective.
* The Committee noted that there was some confusion between the two treatment regimens listed on page 2 of the PIS and the treatment groups listed on pages 3 and 4 of the PIS. They recommended a flow chart or table which clearly differentiates between the age groups and treatment groups to make it more understandable to participants.
* The Committee asked if participants would be given a card outlining their involvement in the study. Ms Low advised that they will inform participants’ GPs and they will be given a pocket card. This has been submitted to the HDEC.
* The Committee asked for scientific peer review that is independent from the sponsor. A suggested template can be found at http://ethics.health.govt.nz/.
* The Committee asked what mitigations were in place to avoid potential conflicts of interest (R.5.4.1) and coercion (P.3.1).
* The Committee asked for clarification on the sample size as this is different in the PIS (n=15) and the application (n=60).
* The Committee requested the following changes to the Participant Information Sheet and Consent Form:
  + Please include a lay title for the PIS (the present title of 5 lines would not be understandable to a lay participant).
  + Please review the PIS for repetition and look at condensing. Bear in mind that it will lay people reading the PIS and any effort to make it more readable and with less repetition and legalese would be appreciated
  + Please amend “you have been asked to participate” to “you are invited” (page 1 of the PIS).
  + Please remove the statement that “your study doctor will be paid for the work carried out in this study” (page 2 of the PIS).
  + Please reconsider the statement “please be informed that the withdrawal of your consent for follow-up will jeopardise the public health value of the study”. We believe this is coercive (page 8 of the PIS).
  + Please provide a lay explanation for the explanation on myocardial ischaemic events, for example if 1,000 people took this drug, X person/people would have a heart attack (page 10 of the PIS). Many participants might not understand percentages.
  + Please move the sentence “Effects potentially associated with the study medication” to the next paragraph and make a heading (page 11 of the PIS).
  + Please include that this study is being sponsored by Boehringer in New Zealand (page 12 of the PIS).
  + Please remove statement that people looking at data will be sworn to strict secrecy (page 13 of the PIS).
  + Please consider reducing the information on “what will happen to information about me?” (page 13 of the PIS).

Decision

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

* Please amend the participant information and consent form, taking into account the suggestions by the Committee *(Ethical Guidelines for Intervention Studies, para 6.22).*
* Please provide independent scientific peer review *(Ethical Guidelines for Intervention Studies, para 5.11).*

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

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| **8** | **Ethics ref:** | **14/NTA/190** |
|  | Title: | Melatonin bioequivalence study conducted under fasting conditions |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Generic Partners Pty Ltd |
|  | Clock Start Date: | 30 October 2014 |

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 ethical issues

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

* The Committee noted that there had been discussions at the last Northern A meeting around the independence of Professor Glue’s peer review. Mrs Folland explained that they are currently trying to find someone but it is not easy. The Committee advised that it would be preferable if the peer review was done by someone who has not previously worked with the company. The Committee was asked if Paul Fawcett could be used. The Committee agreed that he could, providing he was independent of Zenith.
* The Committee noted that changes have been made to the PIS based on previous comments but it was still very wordy and repetitive which makes it difficult for participants to understand.
* The Committee asked why a mouth check would be conducted. Dr Noelyn Hung explained that this was to check that participants had taken the drug.
* The Committee asked why plasma samples would be kept for five years after analysis. Dr Tak Hung explained that this was for the FDA as in some studies overseas, investigators had cheated on the study and cited patient withdrawal as the reason for there being no sample.
* The Committee asked if the photo ID would be destroyed at the end of the study or returned. Mrs Folland advised that it would be destroyed once the study was completed.
* The Committee asked why data would be kept for 25 years. Mrs Folland explained that this was part of Zenith’s standard operating procedure and regulatory requirements for auditing.
* The Committee requested the following changes to the Participant Information Sheet and Consent Form:
  + Please change “will be reimbursed” to “will be paid” (page 9 of the PIS).
  + Please add the word “injury” to “this means that if you suffer” (page 10 of the PIS).
  + Please amend “at least the level of the Accident Rehabilitation Programme” to “at least the level of the Accident Compensation Act” as more than rehabilitation is covered (page 10 of the PIS).

Decision

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

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

This following information will be reviewed, and a final decision made on the application, by Dr Brian Fergus, Ms Michele Stanton and Ms Shamim Chagani.

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| **9** | **Ethics ref:** | **14/NTA/191** |
|  | Title: | Melatonin bioequivalence study conducted under fed conditions |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Generic Partners Pty Ltd |
|  | Clock Start Date: | 30 October 2014 |

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 ethical issues

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

* The Committee noted that this was a similar study to 14/NTA/190 and the same issues applied.
* The Committee requested the following changes to the Participant Information Sheet and Consent Form:
  + Please change “will be reimbursed” to “will be paid” (page 9 of the PIS).
  + Please add the word “injury” to “this means that if you suffer” (page 10 of the PIS).
  + Please amend “at least the level of the Accident Rehabilitation Programme” to “at least the level of the Accident Compensation Act” as more than rehabilitation is covered (page 10 of the PIS).

Decision

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

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

This following information will be reviewed, and a final decision made on the application, by Dr Brian Fergus, Ms Susan Buckland and Dr Mark Smith.

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| **10** | **Ethics ref:** | **14/NTA/192** |
|  | Title: | Melatonin bioequivalence study conducted under fasting conditions and at steady state |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Generic Partners Pty Ltd |
|  | Clock Start Date: | 30 October 2014 |

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 ethical issues

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

* The Committee noted that this was a similar study to 14/NTA/190 and the 14/NTA/191 and the same issues applied.
* The Committee requested the following changes to the Participant Information Sheet and Consent Form:
  + Please change “will be reimbursed” to “will be paid” (page 9 of the PIS).
  + Please add the word “injury” to “this means that if you suffer” (page 10 of the PIS).
  + Please amend “at least the level of the Accident Rehabilitation Programme” to “at least the level of the Accident Compensation Act” as more than rehabilitation is covered (page 10 of the PIS).

Decision

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

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

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

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| **11** | **Ethics ref:** | **14/NTA/193** |
|  | Title: | Pharmacodynamic Effects of a single dose of Anatabine Citrate |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Rock Creek Pharmaceuticals, Inc. |
|  | Clock Start Date: | 30 October 2014 |

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 ethical issues

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

* The Committee noted the prior publicity relating to the sponsor and the recent FDA warning about promoting the health benefits of its two supplement drug formulations.
* This proposed trial will only be carried in NZ and is aimed strictly at assessing the pharmodynamics of anatabine absorption in a single dose, although it does include some efficacy endpoints related to immune function.
* The Committee were concerned that the PIS was potentially misleading as it implied that the study was for a dietary supplement, and a compound found in the food supply, rather than a drug. While these two elements are technically correct, in the context of the proposed trial anatabine is a new drug and should be presented as such. If any comments are made about anatabine in the food supply it would need to be noted that this is in very low amounts, and any discussion of the dietary supplement would need to include that the supplement contains anatabine but that this drug trial is testing anatabine as a drug to examine how it works in the body. They cited the December 2013 from the FDA warning letter regarding these issues.
* The PIS should also be clear that this is a PD trial, has no therapeutic benefit, and will include testing for some markers of immune function (in lay language).The immune tests are outlined in the protocol but not included in the application r.3.10.
* Dr Tak Hung advised that the FDA were not concerned about the safety of the product, but rather the sponsor had made too many claims.
* Dr Tak Hung advised that they had checked with Medsafe who had advised that as long as the supplement is produced under GMP conditions then SCOTT approval was not required. Subsequent advice to the Committee Chair has confirmed this point
* The Committee asked why this study was being conducted only in New Zealand and not the United States. Dr Tak Hung explained that this was due to the ethical process in New Zealand being quicker.
* The Committee noted that previous studies had used smaller doses than this study. Mrs Folland advised that the sponsor had done studies of up to 18mg with no safety concerns. The discussion of risks in the PIS should not include comments about the dietary supplements, but present more fully the risks outlined from previous studies related to anatabine.
* The committee noted that the peer review did not appear to comment on the safety aspects of the proposed dosage. Could the peer review please address this point.
* The Committee asked if there are potential safety issues where the chemicals would effect the immune system. Dr Tak Hung advised that he thought this was unlikely.
* Could the researcher please confirm the dosage levels and comment on how these compare to previous trials.
* The Committee were concerned that the peer review was neither independent nor adequate for a trial of this nature and did not appear to address safety issues. They advised that they prefer to see a rigorous, independent peer review which, for this trial, contains information on the relationship between the dietary supplement and drug with reference to the FDA ruling, what claims and the way it is represented to participants should be, a discussion about adverse events and how these should be presented to participants and a discussion on the side effects. The PIS then needs to be rewritten making it clear what exactly is being tested.
* The Committee suggested that the researchers talk to Joanne Barnes at the University of Auckland who focuses on the safety aspects of natural health products. As a starting point we recommend the use of the Peer Review Form on the HDEC website
* Could the researcher please confirm the product is being made under GMP.
* Turning now to the PIS. Opening paragraph. First sentence OK. Second sentence change. We suggest “Anatabine is a naturally occurring compound in many plants and the citrate form has been used as dietary supplement in a number of dietary supplements. The proposed project is not concerned with supplement issues, rather it is the use of anatabine citrate to enhance the immune system. This is a Phase 1 study looking at how anatabine is absorbed in the body from a single large dose. There will be no therapeutic benefit from this chemical. The risks from this dosage are believed to be low”
* Please provide clarification on section 6 of the PIS where it says “you should be aware for safety and monitoring reasons, the investigator’s room is connected to real time digital monitoring equipment. Is it possible the participants could be identified from the real time monitoring? If yes, then this should be clarified in the PIS.
* PIS. P3, Risks. We note dizziness is only ranked 6th whereas a review of the Protocol showed that 33% of participants (RCP 007) experienced dizziness. Could you review this and express the risks so that participants fully understand the risks.
* PIS. P 6 says the blood samples will be shipped to Rock Creek Pharmaceuticals. Please follow MOH guidelines on shipping blood overseas and explain this more fully in the PIS and CF. It is unclear whether all the blood will be consumed in the test and if there is residual how will it destroyed, or will residual be stored for future research and for how long. Participants have to agree in CF to samples going overseas and being stored there.
* In the application f.1.1 the researchers claim that this trial may reduce inequalities. Please note for future applications that this is a non-therapeutic PD trial of 10 people, and will have no impact on inequalities at this point.

Decision

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

* Please provide independent peer review which addresses the points listed above *(Ethical Guidelines for Intervention Studies, para 5.11).*
* Please amend the participant information sheet and consent form taking into account the points raised above in the peer review *(Ethical Guidelines for Intervention Studies, para 6.22).*
* Please provide evidence of GMP.

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

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| **12** | **Ethics ref:** | **14/NTA/194** |
|  | Title: | Treatment Barriers for Māori with Social Anxiety |
|  | Principal Investigator: | Ms Pixie Armstrong-Barrington |
|  | Sponsor: | Massey University |
|  | Clock Start Date: | 30 October 2014 |

Ms Pixie Armstrong-Barrington and Dr Angela McNaught were present in person for discussion of this application.

Potential conflicts of interest

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

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

Summary of ethical issues

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

* Ms Armstrong-Barrington explained that this study would look at the treatment barriers for Māori with social anxiety, using a qualitative design, face to face interviews and thematic analysis. She said that existing literature shows that there has not been much done with Māori but it is one of the most common disorders among Māori.
* Ms Armstrong-Barrington explained that ethical considerations related to ensuring that the research is culturally appropriate, appreciation and respect of Māori beliefs are maintained, following Māori tikanga, sharing of information, establishing relationships, offering a koha to participants and care around potentially vulnerable participants.
* Ms Armstrong-Barrington advised that she would be conducting interviews as part of her doctorate in clinical psychology but she was not a psychologist.
* The Committee asked what consultation with Māori had been undertaken. Ms Armstrong-Barrington explained that she had consulted with the kaumatua at Massey University, attended fortnightly huis talking about Māori knowledge, had discussions with her cultural supervisor Dr Simon Bennett and engaged with Māori in the community with discussions on how the research might be received. The Committee advised that a letter of support needs to be provided outlining that consultation with Māori has taken place.
* The Committee asked how the results of this study will be published. Ms Armstrong-Barrington advised that it would most likely be in academic journals. She agreed to consider non-academic journals and about how the study can contribute to overall knowledge, for example giving the results to Māori in the psychology department.
* The Committee asked how the number of participants (12) had been decided Ms Armstrong-Barrington explained that a qualitative study required less numbers than a quantitative study and it may be difficult to recruit people with social anxiety.
* Ms Armstrong-Barrington explained that she will approach health organisations and ask them to give brochures to patients who have demonstrated symptoms of social anxiety.
* The Committee asked why Māori had been chosen. Ms Armstrong-Barrington explained that it was because there so was little literature around social anxiety in Māori yet it was so prevalent.
* The Committee asked how participants would be screened in order to have participants with a level of social anxiety that would make the study worthwhile, particularly given that some people with social anxiety wanting to talk will not be accessing services. Dr McNaught explained that even people with mild social anxiety are impaired and they may be showing up with other issues.
* The Committee asked how other co-morbidities would be dealt with. Dr McNaught explained that she had talked with mental health nurses and had asked that people with psychosis be excluded.
* The Committee asked if a 45 minute to one hour session would be tolerable for people who may be quite vulnerable. Ms Armstrong-Barrington advised that the emphasis would be on making participants feel as comfortable as possible.
* The Committee asked what safety processes were in place for the researcher. Dr McNaught explained that the interviews would be conducted at the service provider and that she is a practising clinical psychologist so will discuss risks and how to manage these with Ms Armstrong-Barrington.
* The Committee requested the following changes to the Participant Information Sheet and Consent Form:
  + Please consider a more user friendly title than a clinical title.
  + Please provide contact details for additional Māori cultural support.
  + Please let participants know what will happen to the videos after the study.
  + Please make it clear what role the support person can play.
  + Please include a postal address to contact the research.
  + Please make it clear that people do not have to answer any questions that they feel uncomfortable with.
  + Please include that participants will be given a pseudonym.
  + Please include supervisor contact details.
  + Please add that the study includes a questionnaire.

Decision

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

* Please amend the participant information and consent form, taking into account the suggestions by the Committee *(Ethical Guidelines for Observational Studies, para 6.10).*
* Please provide a letter of support for consultation with Maori *(Ethical Guidelines for Observational Studies, para 4.4)*

This following information will be reviewed, and a final decision made on the application, by Mr Kerry Hiini and Dr Mark Smith

## 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:

|  |  |
| --- | --- |
| **Meeting date:** | 09 December 2014, 01:00 PM |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

No members tendered apologies for this meeting.

1. **Any other business**

The HDEC Secretariat agreed to discuss whether the NHC could peer review device studies.

The meeting closed at 6.20pm