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| **Committee:** | Northern B Health and Disability Ethics Committee |
| **Meeting date:** | 07 February 2017 |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

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| **Time** | **Item of business** |
| 12.00pm | Welcome |
| 12.05pm | Confirmation of minutes of meeting of 8 November 2016. |
| 12.30pm | New applications (see over for details) |
|  | i 17/NTB/7  ii 17/NTB/9  iii 17/NTB/11  iv 17/NTB/13  v 17/NTB/14  vi 17/NTB/15  vii 17/NTB/16  viii 17/NTB/18  ix 17/NTB/19  x 17/NTB/20  xi 17/NTB/21  xii 17/NTB/22 |
| 5,30pm | Substantial amendments (see over for details) |
|  | i NTY/06/07/060/AM06 |
| 5.45pm | General business:   * Noting section of agenda |
| 6.00pm | Meeting ends |

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

## Welcome

The Chair opened the meeting at 12.00pm and welcomed Committee members, noting that apologies had been received from Mrs Stephanie Pollard.

The Chair noted that it would be necessary to co-opt members of other HDECs in accordance with the SOPs. Dr Nicola Swain confirmed their eligibility, and were co-opted by the Chair as members 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 8 November 2016 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **17/NTB/7** |
|  | Title: | Preterm Qual |
|  | Principal Investigator: | Dr Fiona Cram |
|  | Sponsor: | Women's Health Research Centre, University of Otag |
|  | Clock Start Date: | 26 January 2017 |

Dr Fiona Cram 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. This study is a Kaupapa Māori qualitative longitudinal study that examines the experiences of whānau as they journey along the preterm care pathway until one year after delivery.
2. The study examines the experiences, barriers and facilitators faced by these whānau. As well as the impact, this in depth look will inform the researchers of structural and clinical issues that we can address to reduce the burden of disability and harm of preterm birth
3. Health practitioners in 4 DHBs will be engaged to seek out the parents/caregivers of Māori babies in their neonatal units, and ask their permission for the researchers to contact them. The journey of 20 Māori babies born prematurely (24-36+6 weeks gestation) will be followed.
4. Mothers/parents will be interviewed 3-6 times, beginning as soon as possible following their admission to a neonatal unit/s, while baby is in a neonatal unit/s, when baby has been discharged home, and finally when baby is one year old.
5. Mothers/parents may have friends or whānau with them when they are interviewed. In addition, these support people may be interviewed separately (if parents’ consent). Health practitioners involved in the baby’s care may also be interviewed (if parents’ consent) at different points along the care pathway.
6. Data will be analysed using interpretive phenomenological analysis that allows for the bottom-up emergence of themes related to interviewees’ experiences and the meanings they attribute to these. The study goal is service transformation to ensure that whānau are supported as they face the joys and challenges of parenting their precious taonga (precious newborn gift).

Summary of ethical issues (resolved)

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

1. The Committee noted that this research context was highly vulnerable. The Researcher(s) confirmed it was, and explained they heavily rely on those who interact with the potential participants, for example midwives, to ensure participants are in an appropriate situation to be talked to about research. The Researcher(s) added that the midwife is the person who approaches the potential participant and informs the researcher when an appropriate time to make contact is, whether that is 2 weeks or 6 weeks. In some cases they cannot approach due to the potential participant never being in an appropriate space to participate in research.
2. The Committee discussed building rapport with the mums as another mitigation for undue stress. The Researcher(s) acknowledged the importance of a gentle enquiry.
3. The Committee noted two design issues that were of ethical significance: b.2.1 "Research should be well designed to answer the study questions". Having a premature a baby is in itself a distressing and disorienting experience for most mums. As there is no control non-Maori group, The Committee asked how researchers would separate out the parts of the journey that are particular to Maori. The Researcher(s) stated they want to know journey of Whanau through this system. The Committee noted this study is assessed through a Maori lens, however some features of the journey may be ubiquitous – and asked how could you control for features that are shared to know what is unique for Maori. The Committee suggested a historical control, which is not ideal but still give some controlling validity. The Researcher(s) responded that because it is case study research it could define patterns and look for cause and effect within those patterns. The Researcher(s) acknowledged that if it improves a system for Maori and improve the system for vulnerable people generally – it would still improve the system (potentially for all).
4. The Committee noted a sample size of 5 mums from a geographic area seems too small a sample on which to base "transforming" recommendations. The Researcher(s) stated that women report similar stories. The Committee noted it is possible that the DHBs are quite different, particularly in terms of the experiences of ‘the system’. The Committee asked whether 5 participants are enough. The Researcher(s) stated they expect general themes of responsiveness. They chose to go across multiple DHBs to have generalisable results. If all women at one DHB raised something it may be something unique to that area. The Researcher(s) confirmed they were reasonably confident to receive a commonality of response across the DHBs and the general themes reported.
5. The Committee noted the importance of being aware of the research being an intervention and suggested minimising contact as to not avoid the experience of the system. The Researcher(s) noted they believe people increasingly know what research is, and can engage and tell their story accordingly.
6. The Committee noted the answer to R.6.1did not address stigmatisation of neonatal staff. The Committee asked what would happen if negative reports of staff at a DHB would occur during the interviews and subsequent reports. The Researcher(s) stated they plan to consult with each DHB. The Researcher(s) plan to not give the DHB a report, rather they plan to address any problems reported and will feed this information back to the DHB and staff in a collaborative way. The Committee confirmed this approach was appropriate.
7. The Committee asked how audio files from outside Wellington would be uploaded to the safe university server or database. The Researcher(s) stated they would take the recorder to Wellington – this is a physical device.
8. The Committee asked for information about Maori consultation and if Maori interviewers were available. Pehea kua mate ke te pepi? The Researcher(s) confirmed they do have Maori interviewers.

Summary of ethical issues (outstanding)

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

1. The Committee noted this study is dealing with a vulnerable and potentially distressed participant group. The protocol outlines a sensitive path for approaching potential participants but no consideration of how researchers will avoid contacting parents of a baby who has died after discharge. The Researcher(s) stated they find out such information from the midwives, acknowledging some may pass away during or after the interviewing period. The Committee asked whether checking with the GP was another safety check to ensure potential participants are not approached after their baby passes away. The Researcher(s) noted it was possible that the GP could advice as an additional check. The Researcher(s) stated they would add this safety measure in the protocol.
2. The Committee queried whether the researchers were only approaching women who had one (or rather their first) preterm birth. The Researcher(s) stated they would limit the study to those who were experiencing their first preterm birth. Please amend the protocol to add this as inclusion criteria.
3. Confidentiality: b.4.4.1 says data may be given to other researchers in identifiable form. The Committee stated if it is identifiable then consent should for this explicitly. This should be optional and very clear.
4. The Committee requested a signed transcriptionist confidentiality agreement (template).
5. R.7.1 The Committee requested a protocol for keeping researchers safe on home visits. The Researcher(s) acknowledged it would be helpful to formalise this. The Committee suggested contacting AUT or the DHB.
6. The Committee asked what observations were taken in the neonatal unit and how will researchers ensure they only observe those who are participating. The Researcher(s) stated they just want to be there to get the feeling about what is going on, to be knowledgeable. The Researcher(s) don’t plan to write up the experience generally, rather just to observe the consented Whanau context. The Committee requested an observing protocol.
7. The Committee asked for more information about Koha. The Researcher(s) stated it would be food and vouchers.

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

1. PIS for mums - pg. 2 Heading "Why should I participate" a bit coercive. Suggest " What is the study about" or something similar.
2. Pg. 2 "finding" should be " funding".
3. For all of the Participant Information Sheet:
4. PIS health carers - consent clauses 5 and 6 refer to "my medical care" and "my health" Amend to make appropriate for health carers to sign.
5. Add information on contacting participants for up to 5 to 10 years. Currently in the protocol but not in the Participant Information Sheet.
6. Provide options for contacting other members of the family, as well as the doctor.
7. Please include counselling details, customised for each locality.
8. Customise for healthcare workers, currently states ‘use of their health information’. This is not relevant.
9. Include extension number for Maori support details.
10. Include option for interpreter.

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 Observational Studies para 6.10)*
* Provide protocols for additional safety measures as outlined by the Committee.

This following information will be reviewed, and a final decision made on the application, by Mrs Kate O’Connor and Dr Nora Lynch.

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| **2** | **Ethics ref:** | **17/NTB/9** |  |
|  | Title: | The genetics of digestive function |  |
|  | Principal Investigator: | Professor Stephen P Robertson |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 26 January 2017 |  |

Professor Stephen P Robertson was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The study investigates Pancreatic insufficiency. This results from diminished pancreatic enzyme or bicarbonate secretion leading to maldigestion; the clinical hallmark of which is steatorrhoea. In severe cases this can result in failure to thrive, chronic diarrhoea and other non-specific gastrointestinal disturbance. Pancreatic insufficiency can occur in both paediatric and adult patients, and can be inherited. The Researcher(s) understanding of these heritable forms is improving as genomic technologies advance. As such it is possible that previously unrecognised isolated enzyme deficiencies may exist.
2. The Clinical Genetics Group at the University of Otago have identified a local whanau with a genetic deficiency of a specific pancreatic enzyme. In the 1000 Genome Project it has been shown that the same gene deletion seen in the local family is present in 4% of the population - this means that the condition we are interested in could be present in 1 in 625 people, and is a potentially unrecognised disease entity.
3. In collaboration with clinical pathologists, as well as local adult/paediatric gastroenterologists and paediatricians, The Researcher(s) will seek to identify a cohort of participants with otherwise unexplained pancreatic insufficiency. Via the clinician responsible for the participant, we will invite them to our study to voluntarily provide a DNA sample (either buccal swab or blood specimen) to identify the genetic mutation. If the genetic mutation of interest is identified, we will invite the participant to give further information on their symptoms as well as a blood sample for other laboratory markers of pancreatic insufficiency (e.g. micronutrient deficiency), and growth parameters.

Specifically The Researcher(s) aim to:

1. 1) Identify a cohort of participants with pancreatic insufficiency of unclear aetiology (major causes excluded), and to screen for mutations in genes of interest;
2. 2) Characterise the biochemical and clinical presentation of this disorder in this cohort of individuals.

Summary of ethical issues (resolved)

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

1. The Committee queried what the collaboration with an international body was (for use of tissue). The Researcher(s) stated this was to analyse the DNA for the main study, adding this analysis cannot be done in New Zealand.
2. The Committee queried the sample size. The Researcher(s) stated their current plan would provide diagnostic significance. The Committee requested a clarification of what a sufficient sample size would look like. The Researcher(s) stated no way of accurately answering this question at the present time.
3. The Researcher(s) confirmed health information was de-identified for storage during the study.
4. The Committee queried whether tissue would be returned. The Researcher(s) stated they would if it was requested. The Researcher(s) added residuals are returned from overseas. The Committee noted this is good practice.
5. The Committee queried who seeks consent. The Researcher(s) stated primary or secondary care person makes initial approach but the CI will conduct the informed consent process if the person is favourable to be approached.
6. Please provide more numbers than the Dunedin number. The Researcher(s) stated they are starting in the South so the number will be accessible.
7. The Researcher(s) confirmed Ngai Tahu Health Research Consultation Committee has given their support.
8. A.6.2 – The Researcher(s) explained that it is likely that other researchers from around the world would become interested in participating in this study.
9. The Committee suggested the postgraduate office is a sponsor for PhD work.

Summary of ethical issues (outstanding)

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

1. The Committee queried the age range of participants. The Researcher(s) stated newborn to older children (16+). The Researcher(s) noted they had Participant Information Sheets so that the legal guardian could sign for children. The Committee noted there was a parent of children form, an adult form and a 7-11 assent. The Committee noted there could be an assent for younger than 7 if not just to help foster inclusivity.
2. The Committee queried whether there was any storage of tissue. The Researcher(s) confirmed there was a chance of new testing being developed. The Committee noted any future unspecified research needed to be a separate document, please view the Ministry of Health Guidelines for Consent for Future Unspecified Research.
3. The Committee noted the potential distress at having a genetically transmissible disorder identified. The Committee acknowledged this is mitigated to an extent by the benefit of finding an explanation of their disease, noting the researcher is a geneticist who will be well used to dealing with such scenarios. The Researcher(s) confirmed that a genetic counsellor could be used if it was a complex situation; otherwise the participant’s doctor could manage an incidental finding. The Committee requested the process for management of incidental findings was bolstered to the Participant Information Sheet.
4. The Committee queried whether only incidental findings that could be addressed would be raised with participants. The Researcher(s) stated most of the time people see utility in inheritance patterns of these kinds of diagnosis, even if it was not immediately treatable. The Researcher(s) added if there is a clinical disorder identified we offer them hearing about it or choosing not to hear about it, from the beginning of the study. This is outlined in the Participant Information Sheet. The Researcher(s) noted they would not involve participants who choose not to know their incidental findings, noting the ethical issues around this. The Committee requested this is more upfront in the Participant Information Sheet as it is effectively an exclusion criterion.

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

1. Please add more information on the Participant Information Sheet about storage of tissue. See the HDEC checklist for informed consent at <http://ethics.health.govt.nz/>
2. Add Maori support on the Participant Information Sheet, near the HDC contacts.
3. On the consent form – please only have yes/no options if the statement is truly optional.
4. Make it clearer that no treatment will be forthcoming even if a genetic abnormality is found.
5. Please add where tissue going and acknowledge that a New Zealander researcher cannot actually control what goes on in an overseas lab, despite "having custodianship" of the DNA (Not the same as having physical control).
6. Assent documents – The Committee noted there is an honest attempt has been made to supply assent documents but the sole one uploaded, seemingly for 7-11 year olds, is way beyond what many 7 year olds could understand. More suited to the 11-15 year age group. Need to develop a much simpler pictorial document for younger children. Both should have a place to make an assent mark. Some between 11-15 can provide their own consent too.
7. Add contact numbers for 11-15 year olds if they want to seek support. This includes investigators and cultural support.
8. Please put participation to them as an option ‘if you would like to’ regarding genetic information (child Participant Information Sheet). I.e. what happens if I decide to participate?
9. ‘If yes I consent to storage of my samples’ – The Committee asked whether each future use be re-consented. The Committee asked whether you were actually planning to re-consent. The Researcher(s) stated they actually meant they would seek ethical review to re-use but not re-consent. The Committee stated this must be clear to participants, please revise this and remove the statement suggesting re-consent.
10. Add that this study is for a PhD.
11. Revise parent Participant Information Sheet make sure it is consistently referring to the parent.

Adult and parent PIS/CF:

1. Explain what a pancreas is
2. Paragraph on "Genetic Studies" would be better placed later in the document once the actual study has been described
3. Pg. 2- which sort of doctor will explain the results? Your specialist ? Your GP?
4. On adult PIS pg. 2, rethink the use of the word 'malformations'. Doesn't seem appropriate for this study.
5. The Committee requested the compensation wording is updated for accuracy, they suggested the following 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.”*

Decision

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

* Please amend the information sheet and consent form, and assent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Observation Studies* *para 6.11*).
* Please provide suitable information sheets and assent forms. This includes an information sheet and consent form for parents of participants unable to provide informed consent, an information sheet and consent form for participants able to provide their own informed consent (this includes all participants aged 16 years or older and may include some younger participants if they are deemed competent), an information sheet and assent form for children, and a very simple information sheet and assent form for young children that should very simply explain their participation in the study. Guidance on assent can be found at <http://ethics.health.govt.nz/guidance-materials/assent-guidance> (*Ethical Guidelines for Observation Studies 6.21)*
* Please provide a separate Participant Information Sheet and Consent Form for the use of tissue for future unspecified research (*Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes, para 2*).

This following information will be reviewed, and a final decision made on the application, by Mrs Leesa Russel and Mrs Mali Erik.

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| **3** | **Ethics ref:** | **17/NTB/11** |
|  | Title: | Measles Management in Māori |
|  | Principal Investigator: | Dr Karen Wright |
|  | Sponsor: | Waikato DHB |
|  | Clock Start Date: | 26 January 2017 |

Dr Karen Wright was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The purpose of this study is to critically review the effectiveness of public health advice/instructions delivered to Māori measles cases and contacts during the 2016 outbreak. Māori cases and contacts, Māori Health providers, and the Population Health clinical practitioners will be interviewed. Recommendations will be made to make the process around case and contact management more effective for Māori and improve health outcomes.
2. The study aims to:

* Describe the public health advice/information given to Māori measles cases and contacts and methods of communication used in the 2016 Waikato outbreak
* Describe the understanding and effectiveness of the information delivered and method of communication
* Identify factors that support and prohibit Māori cases and contacts from obtaining a positive health outcome with regards to the public health management of measles
* Develop recommendations to make the approach to measles case and contact management more effective for Māori.

1. Findings will influence the current management of Māori cases and contacts of measles and findings will be reported back to the study participants and community.

Summary of ethical issues (resolved)

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

1. The Committee queried how it was determined that Maori had worse care, is it just the burden of disease or is it the quality and kind of care offered. The Researcher(s) stated the main driver is the burden for Maori and also to achieve equity with health outcomes.
2. The Committee noted the screening of public health files to obtain cases/contacts and their contact details. The Committee noted this is justifiable under the Health Information Privacy Code 1994, Rule 11, 2c)iii.
3. The Committee queried whether families might not be able to have discussions about childhood illness, due to transient populations, for example in the Waikato. Not just Maori, but if Maori are transient they may not have senior Maori people to relate to in their community. The Researcher(s) noted this was the kind of information they expected to find out through the research.

Summary of ethical issues (outstanding)

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

1. The Committee noted the peer review is not independent; it comes from a public health physician who helped to design the study. Please obtain outside review of the design, using the HDEC template preferably, found at <http://ethics.health.govt.nz/>
2. The Committee was unhappy with the lead off question in the Health Care Worker's questionnaire- "What understanding do you think Maori cases and contacts have about measles?" It encourages a stereotyped way of thinking about a diverse group of people. The Committee request this is reworded as it implies homogenous views. Please remove it.
3. The Committee requested a transcriptionist's confidentiality agreement.
4. Add two more protocols for visits – do not sit on tables, do not put bags on tables

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

1. Please label each with the CATEGORY of participant to lessen the chance of giving out the wrong one
2. Add the information that the interview will be audio taped.
3. Add that clinical health files will be reviewed for further information.
4. Offer a review of the individual transcript so it can be checked for accurate meaning before it is incorporated into the general summary. This can be optional.
5. Remove tick boxes from consent clauses which are non optional for participation

Participant Information Sheet cases and contacts 12-15 years:

1. The Committee felt these documents were outside the reading age of some 12 year olds. Please simplify. The assent form needs the word 'consent' removed from clauses 6 and 8 as the minor assents but the caregiver consents.

PISC cases and contacts >16 years:

1. The Committee queried why the phrase "because you identify as of Maori ethnicity" been left out of the reasons for involvement on Pg 2, while it is in the other PISs for 12-15 and caregivers. The Researcher(s) stated this was an error.

Participant Information Sheet for Caregivers

1. Modify clause 5 on consent to reflect the signatory is a health care worker not a patient ( currently reads "without affecting my or my child's medical care")
2. Add extension number for Maori contacts number.

Decision

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

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

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

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| **4** | **Ethics ref:** | **17/NTB/13** |
|  | Title: | Study of the Safety and Efficacy of Lemborexant in SubjectsWith Insomnia Disorder |
|  | Principal Investigator: | Dr Dean Quinn |
|  | Sponsor: |  |
|  | Clock Start Date: | 26 January 2017 |

Dr Dean Quinn was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. Currently available pharmacological treatments used clinically for insomnia include benzodiazepines, non-benzodiazepine γ-aminobutyric acid (GABA) releasing agents including GABAA receptor positive-allosteric modulators, antidepressants, melatonin and melatonin agonists, and antihistamines, and other prescription and nonprescription medications with sedative properties. Recently, there has been increased awareness of the need for sleep-promoting agents with new mechanisms of action.
2. Towards this end, research findings have suggested that central nervous system orexin receptors may be suitable targets for novel interventional strategies. This is supported by the recent approval of suvorexant, a drug in the same class as lemborexant which was shown in clinical trials to significantly improve sleep maintenance insomnia, but at the starting dose approved for use, showed suboptimal efficacy, particularly on sleep maintenance.
3. Phase 1 and Phase 2 studies in the lemborexant clinical program have provided evidence for pharmacological efficacy at safe and well-tolerated doses.
4. The present study is designed to provide evidence from a large sample of subjects with insomnia disorder, that lemborexant is effective at doses that are safe and well tolerated and that do not cause meaningful morning sleepiness.
5. This study will be part of the Phase 3 clinical study program, which is intended to support planned marketing applications.

Summary of ethical issues (outstanding)

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

1. The Committee noted the absence of any formal data monitoring committee other than one specifically set up to monitor for cataplexy. The justification given for no DMC was not convincing. The Committee noted that to date, the longest period on the drug has been 15 days (N=235). This study will have participants on the drug for 365 days - the participants will include 40% > 65years, a physically vulnerable group particularly where sedatives are concerned (falls/fractures, confusion or other reactions in an aging brain) - there are reports among the ~ 460 Phase1/11 participants of cataplexy, sleep paralysis (~5%), several cases of reduced night time oxygen saturation and one case of multiple grand mal seizure. For these reasons the Committee do not accept that this is a drug unlikely to harm any participants as claimed.
2. The Researcher(s) stated there is the usual safety reporting (SE SAE etc) will occur, explaining they think existing monitoring was appropriate. The Committee asked if the researcher felt there was risk in relation to the previous points. The Researcher(s) stated no risk per se, there are mitigations in the protocol and participant? Information sheet that considered safety.
3. The Committee noted there seems to be little consideration about what may happen once the drug is discontinued after 12 months continuous use, explaining sleeping drugs, when withdrawn abruptly, are commonly associated with rebound sleep disturbance which can be severe. The Committee explained that this won’t necessarily manifest itself after brief drug exposure so the fact that 235 subjects took it for 2 weeks then stopped is not enough reassurance.
4. The Committee requested the sponsor consider adding increased monitoring. Please justify why monitoring is not required or provide a DSMC.
5. The Committee requested some warning about possible rebound sleep disturbance in the PIS..
6. The Committee noted SCOTT would decide whether this constitutes a potential safety issue other than worsened sleep. The Researcher(s) noted there was no evidence of rebound insomnia or withdrawal effects.
7. The Committee noted driving vehicles might be a risk if participants are on sedatives for so long. The Researcher(s) confirmed it could be, but people need to be aware of these effects and these risks and they need to be balanced.
8. The Committee requested that the Participant Information Sheet contains a stronger warning than the current "use of machinery" phrase. This is a potential public safety issue.
9. The Researcher(s) acknowledged the placebo wording is confusing in Participant Information Sheet – please simplify. I.e. two opportunities to swap over from what you are on.
10. The Committee noted the use of a placebo for 6 months has been adequately justified.
11. There are an extraordinarily large number of questionnaires to complete multiple times. The Participant Information Sheet could allude to this with an approximate time frame it will take each time to complete them
12. HDCE form: G. The Committee queried why the answer is "no" to the use of health information. The Researcher(s) stated this was an error.
13. r.1.8 "anaemia" or "insomnia"? p.3.1 Talk me through how participants will be identified in each of the 4 centres. I am not clear on this.
14. p.3.3.1 Re "reasonable amount" for travel reimbursement, please clarify what is reasonable.

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

1. Pg. 2 " flip of a coin" simile is illogical for a 3-arm trial
2. Pg. 7 -Risks to pregnant women- 2nd line last para "of" should be "and"
3. Pg. 10. Complaints. What is the "research centre complaint procedure" and how is it accessed. Please clarify.
4. Add ‘New Zealand courts’ to compensation section, as well as complaint section. Page 10. Be more explicit than ‘the hospital’.
5. Explain why samples may go to PPD and what will happen to samples.
6. Page 12 – more definition around what reasonable means.
7. Ensure details are included for Maori health support.
8. Page 11 – add options for emergency unblinding.
9. Remove ‘ethical opinion is favourable’. Just state we have approved it.

Decision

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

* Provide details of the Data Safety Monitoring Committee’s composition and monitoring plan *(Ethical Guidelines for Intervention Studies para 6.50).*
* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).

This following information will be reviewed, and a final decision made on the application, by Dr Nora Lynch and Miss Tangihaere Macfarlane.

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| **5** | **Ethics ref:** | **17/NTB/14** |
|  | Title: | A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Safety and Efficacy of Selonsertib in Subjects with Nonalcoholic Steatohepatitis (NASH) and Bridging (F3) Fibrosis |
|  | Principal Investigator: | Dr. David Orr |
|  | Sponsor: | Gilead Sciences Pty Ltd |
|  | Clock Start Date: | 26 January 2017 |

Dr. David Orr was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This is a Phase 3 double blind placebo controlled randomised controlled trial of a novel selective kinase inhibitor (selonsertib) which is aimimg to limit progression and possibly reverse liver fibrosis of nonalcoholic steatohepatisis for which there is currently no specific drug treatment.
2. New Zealand will have 2 centres and expects to enrol 4 of the 800 participants. Participants will be randomised to one of 2 active treatment arms (18mg or 6 mg) or placebo for the entire 240 weeks of study. If an adjudicated clinical event indicative of liver failure occurs, or fibrosis has progressed from F3 (bridging fibrosis) to F4 (cirrhosis) on the week 48 liver biopsy, participants will be offered open label 18mg active treatment in an OLE to 240 weeks.
3. The drug has been tested in 72 NASH subjects in a Phase 2 study with 43% on the 18mg dose showing regression of fibrosis. Around 450 subjects with other fibrotic conditions have also been through Phase 2 studies.

Summary of ethical issues (resolved)

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

1. The Committee noted the sponsor’s insurance certificate expires November 2017 for a study going to 2022. This will be renewed and submitted with the annual progress reports.
2. The Committee noted the onerousness of being on the placebo, of which 1/5 of the participants are on, for 240 weeks. As well as no potential benefit from the novel drug, these participants will undergo 2 or 3 liver biopsies and make 32 clinic visits.
3. The Committee noted that while this drug's efficacy is not proven, the Phase 2 NASH study of 72 people showed twice as many people on drug had fibrosis regression. Given the lack of an alternative drug for standard care, one could argue for the placebo arm on the basis, as the researchers point out, that trial participation will mean more encouragement to lose weight and eat well which are therapies in themselves.
4. The Researcher(s) confirmed New Zealand is participating in 2 of the 4 sub studies (genomic and unspecified future research substudies but not HepQuant and intensive PK studies).
5. The Researcher(s) explained there is a difficulty with coming up with effective treatment that involves a trial that is less than 12 or 24-months, which are too short to show effective response as regression takes years. Regression is the end point for this trial and because there is no standard of care they must compare against placebo.
6. The Committee accepted the placebo arm justification.
7. The Committee discussed with the researcher whether the risk of 1:10,000 deaths after biopsy is an accurate figure for patients with F3 fibrosis. The Researcher(s) stated anyone with not normal platelet counts are excluded. The Researcher(s) confirmed the figures are accurate.

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

1. The Committee requested that the Participant Information Sheet is strengthened with respect to highlighting the long period on placebo with invasive monitoring tests.
2. The Committee noted informing the GP of study participation is optional and asked if this is safe in a 5 year study of a novel drug. The Researcher(s) stated if patient requested they didn’t want their GP to be informed they wouldn’t, noting they never had such a patient. The Committee stated should not have patient in study if they refuse for their GP to be informed. Please remove this as an option.

General comments:

1. Add lay title
2. Remove from Main, Genomics and FUR documents, the following statements relating to access to health data and withdrawal from study: " By signing this form, you agree that you will not be able to have access to your personal health information related to this study until the study is over "- This is effectively trying to sign away rights in law " You may revoke authorisation of the collection and use of information about you by informing the study doctor in writing." Note that similar statements appear 3 times in the FUR PIS and all need to be expunged
3. Main PIS: Pg. 2 - "flipping a coin" cannot randomise in a 3-arm trial.
4. Remove Pg12 - storage of samples- make clearer that FUR is the subject of a separate PIS. A statement such as "This will only be done for participants who have read and signed a separate informed consent document" would help.
5. Pg. 12 Sending samples overseas. Provide details of which lab and country they will go to.
6. Pg17- typo-'afterafter'
7. Pg 18- typo- 'Tthis'

Optional Genomic Research PIS:

1. Rationale and storage are well described. The statement on excluding pregnant/breastfeeding women is not needed since such women will not be allowed in the Main study. Please remove it.
2. Future Unspecified research PIS Pg 2 indicate where the "central laboratory" is located Pg 4 " The biological samples that are part of this future research test will be provided at no cost to you" . Makes no sense. Unless researcher can justify, remove. Pregnant partner PIS Add a Maori contact
3. Remove from consent, signing authority for legal representative. All participants are over 18 years.

GP Letter

1. "Participants who experience a clinical event prior to completing week 40 of the randomised phase will be offered the option of roll over to the open label extension". Explain what is meant by a "clinical event"
2. What is "TZD"?
3. Mention participants will be having liver biopsies
4. Americanisms – please proofread.

Decision

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

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

This following information will be reviewed, and a final decision made on the application, by Dr Nora Lynch and Mr John Hancock.

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| **6** | **Ethics ref:** | **17/NTB/15** |  |
|  | Title: | A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Safety and Efficacy of Selonsertib in Subjects with Compensated Cirrhosis due to Nonalcoholic Steatohepatitis (NASH) |  |
|  | Principal Investigator: | Dr. David Orr |  |
|  | Sponsor: | Gilead Sciences, Australia & New Zealand |  |
|  | Clock Start Date: | 26 January 2017 |  |

Dr. David Orr was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This study is a mirror image of 17/NTB/14 except the participant population have more advanced liver fibrosis: they have reached the classification of cirrhosis (F4 fibrosis) whereas the previous study will use participants at the F3 (bridging fibrosis) level.

Summary of ethical issues (resolved)

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

1. The Committee noted the sponsor’s insurance certificate expires November 2017 for a study going to 2022. This will be renewed and submitted with the annual progress reports.
2. The Committee noted the onerousness of being on the placebo, of which 1/5 of the participants are on, for 240 weeks. As well as no potential benefit from the novel drug, these participants will undergo 2 or 3 liver biopsies and make 32 clinic visits.
3. The Committee noted that while this drug's efficacy is not proven, the Phase 2 NASH study of 72 people showed twice as many people on drug had fibrosis regression. Given the lack of an alternative drug for standard care, one could argue for the placebo arm on the basis, as the researchers point out, that trial participation will mean more encouragement to lose weight and eat well which are therapies in themselves.
4. The Researcher(s) confirmed New Zealand is not participating in 2 of the 4 sub studies.
5. The Researcher(s) explained there is a difficulty with coming up with effective treatment that involves a trial that is less than 12 or 24-months, which are too short to show effective response as regression takes years. Regression is the end point for this trial and because there is no standard of care they must compare against placebo.
6. The Committee accepted the placebo arm justification.
7. The Committee discussed with the researcher whether the risk of 1:10,000 deaths after biopsy is an accurate figure for patients with F4 fibrosis. The Researcher(s) stated anyone with not normal platelet counts are excluded. The Researcher(s) confirmed the figures are accurate.

Summary of ethical issues (outstanding)

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

1. The Committee noted participants in this study, compared with the previous study 17/MTB/14, are at greater risk, with or without the study, of having a "clinical event" i.e. developing a sign of liver failure. The design, number of New Zealand participants and conduct of the trial is identical as 17/NTB/14.
2. The Committee noted Selonsertib has not been trialled in any Phase 2 study in patients with cirrhosis. Therefore there is no direct evidence of benefits or risks, only that which can be extrapolated from drug use in patients with noncirrhotic fibrosis.
3. The Committee noted there is still a question mark from Phase 1/2 trials, as to whether the drug might cause significant liver test disturbance and if so, what does this mean for participants. The issue is whether this trial of 800 cirrhotic patients should be started before there is either a Phase 2 trial in cirrhosis, or the Phase 3 trial in F3 bridging fibrosis has been allowed to go part way to provide some more definitive evidence of benefit so as to justify trialling it in the more vulnerable cirrhotic group.
4. The Researcher(s) stated there was no evidence for accelerated decompensating from selonsertib. The Committee noted this was in non-cirrhotic population. The Researcher(s) stated when these trials run together, those found ineligible for 17/NTB/14 because of biopsy evidence of early cirrhosis, are still candidates for intervention and treatment in this study, as opposed to waiting for 5 years for first study to be done?. The Committee noted this is not yet known to be an effective treatment. The Researcher(s) reiterated earlier phase research did not show any risk factors. The Committee stated some did show raised liver functions, yet no liver damage. The Committee asked whether for someone with a damaged liver this could be an issue. The Researcher(s) stated they are relaxed as can be while taking into account any risks of giving a patient with a cirrhotic liver any drug. The Researcher(s) stated with all the data monitoring going on any raised liver issues would be picked up. The risk is very low for this group of patients. The Researcher(s) acknowledge it is not tried in this group of patients.
5. The Researcher(s) stated the group that would potentially benefit the most from this drug is the 17/NTB/15 (l4) group.
6. The Committee noted the argument made by the researcher and took into account safety and monitoring information. The Committee also noted the benefit for F4 participants. The Committee requested more justification from the sponsor as to why this trial cannot be started in a staggered start compared to tandem enrolment.

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

1. The Committee requested that the Participant Information Sheet is strengthened with respect to highlighting the long period on placebo with invasive monitoring tests.

General comments:

1. Add lay title
2. Remove from Main, Genomics and FUR documents, the following statements relating to access to health data and withdrawal from study: " By signing this form, you agree that you will not be able to have access to your personal health information related to this study until the study is over "- This is effectively trying to sign away rights in law " You may revoke authorisation of the collection and use of information about you by informing the study doctor in writing." Note that similar statements appear 3 times in the FUR PIS and all need to be expunged
3. Main PIS: Pg. 2 - "flipping a coin" cannot randomise in a 3-arm trial.
4. Remove Pg12 - storage of samples- make clearer that FUR is the subject of a separate PIS. A statement such as "This will only be done for participants who have read and signed a separate informed consent document" would help.
5. Pg. 12 Sending samples overseas. Provide details of which lab and country they will go to.
6. Pg17- typo-'afterafter'
7. Pg 18- typo- 'Tthis'

Optional Genomic Research PIS:

1. Rationale and storage are well described. The statement on excluding pregnant/breastfeeding women is not needed since such women will not be allowed in the Main study. Please remove it.
2. Future Unspecified research PIS Pg 2 indicate where the "central laboratory" is located Pg 4 " The biological samples that are part of this future research test will be provided at no cost to you" . Makes no sense. Unless researcher can justify, remove. Pregnant partner PIS Ad a Maori contact
3. Remove from consent, signing authority for legal representative. All participants are over 18 years.

GP Letter

1. "Participants who experience a clinical event prior to completing week 40 of the randomised phase will be offered the option of roll over to the open label extension". Explain what is meant by a "clinical event"
2. What is "TZD"?
3. Mention participants will be having liver biopsies
4. Americanisms – please proof read. Ex pg.19 – Participant Information Sheet
5. Remove ‘As required by US law’.

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Provide further information on the study design, *in particular starting the study prior to completion of the study in less vulnerable populations* (*Ethical Guidelines for Intervention Studies para* 5.4)

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

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| **7** | **Ethics ref:** | **17/NTB/16** |  |
|  | Title: | LOTUS Study |  |
|  | Principal Investigator: | A/P Catherine Byrnes |  |
|  | Sponsor: | Menzies School of Health Research |  |
|  | Clock Start Date: | 26 January 2017 |  |

Catherine Byrnes and Charmaine Mobberley were present in person for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This study involves a single visit of children enrolled in one of two previous short-term bronchiolitis or long-term bronchiectasis studies where an anti-inflammatory and antibiotic agent 'azithromycin' was trialled against placebo as an intervention. This follow-up will record the outcomes from having these respiratory diseases early in life, and determine the long-term impact of this intervention including whether there is any persisting bacterial resistance.
2. The results will improve understanding on clinical predictors of lung health or ongoing disease in Indigenous children and will inform future management.

Summary of ethical issues (outstanding)

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

1. The Committee noted the blurring of research and therapeutic assessment in Study 2, explaining that the participants come in from time to time for review. The Participant Information Sheet notes if they come for this research visit and are unwell, they may be x-rayed and treated. This would be the correct management of the situation but by putting this in the Participant Information Sheet, it may induce participation in research in order to get clinical assessment. The Committee would like to see this removed from the Participant Information Sheet so that clinical care and optional research are clearly separated in the mind of potential participants.
2. The Committee noted that swabs are being sent to Australia. It is unclear whether swabs from those not signed up for the future unspecified research (FUR) substudy, are going off shore. The Participant Information Sheet says testing is at Starship unless FUR consent signed but a.1.6 says "Samples will be sent from all sites to a single expert laboratory". Please clarify, and if all samples are sent off shore, add this information to the PIS Parent/Caregiver. The Researcher(s) confirmed all original testing is sent to Menzies.

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

**PISC Parent/Guardian**

1. The Committee would like a separate Study 1 and Study 2 PIS for 2 reasons: i.it is confusing to have to read about a study that didn't involve your child, especially as likely some parents will have ESOL or reading difficulties so keep information to what they need to know. ii. while the Study 2 children have a continuing association with the clinic, the Study 1 children have been returned to GP care. Therefore, the PIS as it stands is trying to cover both situations and it makes it less useful for both groups. The Committee noted it would only take a little tweaking to turn it into and a and b version.
2. Pg. 1 Typo 2nd to last para- remove extra 'if'
3. Pg. 2 Explain ‘sputum' and 'lung function' maybe add a picture of someone blowing into a spirometer.
4. Consent form- add witness statement to Investigators signatory panel
5. Pg. 3 A fuller explanation of what costs are covered and how to access this
6. Consider limiting ‘any cost to the family will be reimburse’ – clarify this.

**Child Assent**

1. Add age range 7-11
2. Consider adding a picture of a 'nasal swab'

**Future unspecified Research**

1. Expand on cultural issues, using either your own words the committee recommended the following statement: “*You may hold beliefs about a sacred and shared value of all or any tissue samples removed. The cultural issues associated with sending your samples overseas and/or storing your tissue should be discussed with your family/whanau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult prior to participation in research where this occurs. However, it is acknowledged that individuals have the right to choose.”*
2. Remove tick box for use of tissue for FUR. It is the point of the document.
3. Add extension number for Helen Wihongi on all Participant Information Sheet
4. Pg. 2 – ask you again if we do any test in future. 1: if stored for long period could be hard to recontact for consent, and some children will move to adult. The Committee and The Researcher(s) discussed this and decided that participants should be re-consented at 16 for continued storage and those at 15 can provide their own consent with their parents co-signing, noting they are competent to provide their own consent.

Decision

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

* Please amend the information sheet and consent form, and assent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Observation Studies* *para 6.11*).

This following information will be reviewed, and a final decision made on the application, by Dr Nora Lynch and Miss Tangihaere Macfarlane.

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| **8** | **Ethics ref:** | **17/NTB/18** |  |
|  | Title: | A 3-Year Follow-up Study in participants previously treated with Odalasvir and AL-335 With or Without Simeprevir for Hepatitis C Virus (HCV) Infection. |  |
|  | Principal Investigator: | Dr Catherine Stedman |  |
|  | Sponsor: | Jannsen Cilag (New Zealand) Ltd |  |
|  | Clock Start Date: | 26 January 2017 |  |

Dr Catherine Stedman was not present for discussion of this application.

Potential conflicts of interest

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

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

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

1. Pg. 2 Define APRI.
2. Pg. 3 The way the tests are listed and described makes it appear a liver biopsy is part of the standard assessment although it is not. Reread and adjust to clear up misperception.
3. Pg. 5 Under heading " Alternatives to Participation", is the following sentence: " The alternative drug combination that is best suitable for you will depend on your medical condition including the pattern of resistance at the time of failure" Not only does it not seem clear what "pattern of resistance at the time of failure" might mean to a lay person, many in the study have not failed treatment.
4. Amend Pg. 5 " What will happen to samples" State where Covalence Central is.
5. Remove discussion of FUR as it becomes confusing as to whether this consent is covering it. (just mention it is the subject of another Participant Information Sheet)
6. Avoid cross referencing between Participant Information Sheet. These must be standalone documents.
7. Localise the procedures, i.e. if fibroscan no need for biopsy.

Decision

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

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| **9** | **Ethics ref:** | **17/NTB/19** |  |
|  | Title: | Improving Management of Atrial Fibrillation in Primary Care |  |
|  | Principal Investigator: | Prof Ralph Stewart |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 26 January 2017 |  |

Prof Ralph Stewart was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This is a nationwide general practice, cluster randomised two part study seeking to see if using one of two electronic decision making systems-EDS- (one based on clinical measures, one adding 2 blood-test derived biomarkers to clinical measures) compared with usual clinical decision-making, will:
2. Part 1- improve the rate of prescription of oral anticoagulants for atrial fibrillation patients who meet specified criteria i.e. should be on them according to current best practice. Here, the clinical and biomarker EDSs will issue a recommendation to start oral anticoagulant drugs (OAD) or not. The outcome measure will involve linking encrypted NHIs to the Pharmaceutical Benefits prescription database.
3. Part 2 - improve the 4-year outcome with regard to stroke, bleeding, cardiovascular outcomes generally and death. Here, the Clinical EDS will advise on whether to start OAC/how to minimise bleeding/how to manage rate of AF/management of CV risk. (All part of NICE cardiology guidelines) The Biomarker EDS will also do all this but also suggest treatment changes that are not yet part of cardiology guidelines although underpinned by 2 large trials. These include considering starting OAC even where clinical calculators do not recommend this action (CHA2-DS2-Vas <2), altering BP meds and adding spironalactone (diuretic-BP lowerer). Linking encrypted NHI with prescription database hospital discharges and national mortality databases will derive this outcome.
4. Part 1:N=60 practices 3 arms: Clinical EDS vs Biomarker EDS vs usual care
5. Part 2: N=100 practices aiming for 3000 participants 2 arms: clinical EDS vs biomarker EDS
6. There will be purposive enrichment for low decile and Maori-predominant practices.
7. This is an individual participant-consented study but the consent is verbal and follows the delivery of limited written information by the GP There will be 4 subsequent focus groups, predominantly in Maori areas where participant acceptability of the EDS and retention/understanding of explanations given, will be evaluated.

Summary of ethical issues (resolved)

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

1. The Committee noted standard of care was clinicians making their own clinical decisions that varied considerably. No intervention to clinical decision-making is the first arm of the study. The second arm was the electronic decision support system. The third is electronic decision support system plus blood tests.
2. The Committee noted practices that don’t support electronic decision systems are excluded. The Committee asked what proportion of healthcare systems are not able to participate for this reason. The Researcher(s) stated 80% have the correct system (Medtech) and can participate if they wish. The Committee ask why the 20% that don’t have the electronic system can’t be the control group. The Researcher(s) stated those randomised to the usual care (no intervention) group be randomised after 6 months to one of the other 2 strategies. The first 6 months determines the primary outcome measure.
3. The Researcher(s) confirmed the randomisation is at the practice level (whole DHBs are randomised). I.e. if it is biomarker arm, participants will be given a blood test, they will be informed why; this can be with the routine blood test. This test will be used to inform decision-making. It is as if the blood test is part of usual care, but we are only recommending it in the Biomarker EDS group. Other groups could do one if clinically determined, but the researchers are not actively recommending it if they are not in the blood test arm.
4. The Committee queried if electronic decision software had been created. The Researcher(s) confirmed it had been upgraded to be adapted for this study. It can be modified again for the information related to the blood test results.
5. The Committee noted the study is effectively formalisation of something that is available but not commonly used. The Researcher(s) added there are similar tools available for clinical use, but that an audit revealed low use of the tools. In this study we will encourage use of the tools by way of payment (reimbursement).
6. The Committee queried whether payments would be to the practice or the individual doctor. The Researcher(s) stated an amount for each participant randomised to study will be paid to the practice, adding the sum is modest that mainly covers costs.
7. The Committee stated they were satisfied that this study was standard of care verses standard of care plus additional support. The Committee was satisfied that all parts of the study were informally available irrespective of study participation.
8. The Researcher(s) and The Committee discussed the difficulties surrounding the cluster level randomisation and the use of individual patient data and blood for the study, noting while individual consent was to be sought and information given about the study, the Researcher(s) felt the ‘study’ as far as the cluster section was concerned, was about system quality improvement.
9. The Committee noted importance to remember that health information is the patients. The Researcher(s) acknowledged this point.
10. The Researcher(s) explained the key component was to maintain the Dr-patient relationship.

Summary of ethical issues (outstanding)

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

1. The Committee noted is this randomisation ‘without consent’ due to the individuals receiving clinical care due to the cluster level randomisation, or at least the clinical decision making is influenced by the study.
2. Further, the Biomarker EDS group are potentially to be offered treatment interventions which are not standard care in this context (eg offering OAC when the common clinically-based calculation produces a figure of <2 which normally means no OAC; eg adding spironalactone for AF). The Committee noted that this is also not disclosed to the participants. There is a therapeutic difference in the study arms.
3. The Researcher(s) stated disclosure might undermine the study as it aimed to replicate standard care environments. The Committee interjected that they are in a randomised trial and this must be disclosed.
4. The Researcher(s) acknowledged they don’t know what arm is better or worse (in relation to modification of the biomarker Participant Information Sheet).
5. Generally they could add all arm information to the PIS and state the researchers do not know what the best method is, hence the research.
6. The Committee noted GP payments per capita on provision of complete data (r.5.5.1) This could be understood as an inducement and should be replaced with a per practice payment for time and effort based on a projected number of enrolments and time. This may require changes to the protocol but not the HDEC application form.
7. Obtaining assent from "responsible people where appropriate" (p.3.2.2.2) is not appropriate as children are not likely participants and there is no legal basis to support this. Please remove this. The Committee stated that it is not possible for HDECs to approve an application unless it is consistent with New Zealand law, including the right not to be subjected to medical or scientific experimentation without that person's consent (section 10 of the New Zealand Bill of Rights Act 1990). Research involving participants who are not competent to consent is inconsistent with the Bill of Rights unless it is undertaken in accordance with Right 7 (4) of the of the Code of Health and Disability Services Consumers’ Rights. In addition to requirements regarding ascertaining the views of the consumer and other suitable persons (forms consistent with this aspect are currently included in this application), Right 7(4) of the Code requires that any health services provided without the informed consent of the consumer must be in the best interests of the consumer. This means that there must be some benefit, or potential benefit, to the participant beyond what they would receive if they were not participating in the research.
8. The Committee notes that proxy consent is only legally acceptable in cases where the medical experiment would save the person’s life or prevent serious damage to the person’s health.
9. The Committee requested those who can’t provide their own consent are excluded.
10. The Committee requested the Participant Information Sheet for the focus groups. The Committee noted they can accept the current protocol if the Participant Information Sheet for focus groups are not conducted until submission to HDEC via an amendment. The Researcher(s) stated they prefer this option.
11. The Committee noted that extra patient’s visits resulting from the study and incurring them in additional cost, should be reimbursed to the patient (for further tests required by study participation). Make sure this goes to patient through the practice.

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

1. The focus groups, assembled by Maori managers, will still need a simple PISC and an outline provided to us of the discussion content/process
2. The Researcher(s) stated they would revise Participant Information Sheet to clearly cover the randomisation and the use of data.
3. The Committee felt that there could be a lot more information to be given to ensure free and informed consent, in particular about the higher-level cluster randomisation and the interventions in the different arms of the trial..
4. The Researcher(s) stated if patient doesn’t want to participate in any aspect of the study they don’t have to – they would get regular care from the GP. The Committee noted this should be very clear to participants.
5. The Committee noted patients have two levels of permissions in this study. One is to receive the care the community is randomised to; the other is about health information and pharmacy information being used for the study. If both are individual opt outs it requires much more information to be given to participants.

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Address outstanding ethical issues in a cover letter.

This following information will be reviewed, and a final decision made on the application, by Dr Nora Lynch and Mrs Kate O’Connor.

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| **10** | **Ethics ref:** | **17/NTB/20** |  |
|  | Title: | TextNudge for Activity |  |
|  | Principal Investigator: | Ms Nicola Saywell |  |
|  | Sponsor: | Aucklnd University of Technology |  |
|  | Clock Start Date: | 26 January 2017 |  |

Ms Nicola Saywell and Dr Denise Taylor were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This project investigates whether low-cost accessible technology can ‘nudge’ behaviour change. Previous research suggests that the use of small nudges can lead to behaviour change in a variety of health conditions, including when these are brief, automatically generated text messages.
2. TextNudge for Activity, is an automated text messaging service designed to encourage continuation of prescribed exercises and activity after discharge from community physiotherapy. The team at the National Institute for Health Informatics (NIHI) have developed a system that is easy for therapists to use to allow automated text messaging. The intervention would be offered to all patients discharged by community physiotherapists recruited to the study from Waitemata DHB (aim 6-7) during a 4-week period.
3. The 12-week programme involves texts being sent to each participant daily for the first 4 weeks, then 3 times per week for the remaining 8 weeks. The percentage of potential participants who consent will be recorded and post-intervention interviews will explore participant satisfaction.
4. The research officer will manage a sample of participants who will wear a StepWatch activity monitor for a 1-week period in the 1st and 12th weeks. Daily step count would provide information about the potential effective on physical activity that can be further explored in the full study

Summary of ethical issues (resolved)

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

1. The Committee asked for more information about the monitors. The Researcher(s) explained that they are standard monitors, noting adverse events to participants skin is taken into account, and if someone doesn’t want to use one they can still be part of the study.
2. The Committee queried it is an inducement giving participants mobile phones. The Researcher(s) stated not they are not the latest phones, adding they are not smart phones. The Researcher(s) noted some do not have access to a cell phone and it is important to include this group. The Committee noted that this was justifiable and allowed more participants to be involved.
3. The Researcher(s) explained the plan to recruit. The researchers will first consent staff who will then recruit their patients. The idea is that it reflects normal care as much as possible for community physiotherapists.
4. The Committee noted this is research not service and this should be very clear to participants. The Researcher(s) noted under the benefit section in the participant information it is clear that there may or may not be a benefit.
5. The Researcher(s) clarified that physiotherapist participation is required to recruit patients. This is due to assessment of burden of this potential intervention for physios as part of the study outcomes.
6. The Researcher(s) confirmed that these participants live independently in a community. The Committee stated that all participants must have capacity to consent. The Researcher(s) stated if they live independently they should have capacity but acknowledged it would be appropriate to have a cognitive screen to be sure and confirmed they would exclude anyone who could not consent for themselves.

Summary of ethical issues (outstanding)

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

1. The Committee requested independent peer review that addresses scientific methods.
2. The Researcher(s) confirmed they do already have information about who said STOP (to cease the texts) but wanted more information about reasons for stopping. The Committee noted people don’t have to give a reason for withdrawing from study. The Researcher(s) stated they could rephrase the question to make this clear.
3. The Researcher(s) confirmed the researchers attach the monitor in the participant’s own home. The Committee requested that the researchers submit a site safety protocol for entering people’s homes as a safety measure for researchers. The Committee suggested the researchers look at the AUT ‘keeping ourselves safe’ guidelines as a reference.
4. Please submit amended questions for interviews, as it appears they are not final copies.

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

1. The Committee noted Maori support first says talk to your whanau. It should be an option but not required.
2. PICF (Staff) request consent to get staff health information, but you should not need this as it is not a measure of your intervention. The Researcher(s) confirmed that this was an error. Please remove it from the Participant Information Sheet.
3. The Committee noted the consent form only needs yes or no tuckboxes for statements that are truly optional.
4. Explain jargon (eg. EDARS).

Decision

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

* Please provide evidence of favourable independent peer review of the study protocol (*Ethical Guidelines for Intervention Studies* Appendix 1).
* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Provide final questionnaires and safety protocols.

This following information will be reviewed, and a final decision made on the application, by Mrs Leesa Russell and Mr John Hancock,

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| --- | --- | --- | --- |
| **11** | **Ethics ref:** | **17/NTB/21** |  |
|  | Title: | The effect of cold pressed snack bars on appetite in healthy adults |  |
|  | Principal Investigator: | Dr Christine Butts |  |
|  | Sponsor: | Plant and Food Research Ltd |  |
|  | Clock Start Date: | 26 January 2017 |  |

Dr Christine Butts was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This is a randomised, controlled, cross-over clinical intervention study.
2. The cross-over design will be completed using one negative control snack bar with no red grape skin extract and two test cold pressed snack bars each containing red grape skin extract at two different levels. All three snack bars have the same formulations other than the amount of red grape skin extract.
3. Participants will be required to attend the clinical trial facility at Plant & Food Research, Palmerston North, New Zealand on four (4) occasions over a 3-4 week period. This includes an initial screening visit and blood test and three testing visits.
4. On each testing visit a snack bar will be consumed 15 minutes prior to a standard breakfast of commercial muesli and skim milk. After 240 minutes (4 hours) the participants will be offered a pre- weighed ad libitum lunch which will re-weighed after consumption. Once this is completed participants are free to resume their normal activity.
5. During the study period, participants will be asked to rate their level of satiety following each of the baseline and test meals at set time periods using VAS. They will also be asked to complete a sensory survey after consuming the snack bar.

Summary of ethical issues (resolved)

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

1. The Committee noted a similar study was already approved by HDEC. The Researcher(s) explained the differences. The Committee noted the differences were minor.
2. The Researcher(s) confirmed no side effects were expected.
3. The Committee query if participants liked it could they get ingredients? The Researcher(s) stated yes.
4. Confirmed summary of research results is sent to participants.

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

1. Remove the tick boxes – only have yes and no if the statement is truly optional.
2. Remove second and third line regarding Maori support section. Add extension number too.
3. ‘ad libitum’ – use English.

Decision

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

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| --- | --- | --- | --- |
| **12** | **Ethics ref:** | **17/NTB/22** |  |
|  | Title: | (duplicate) A pilot randomised control trial (RCT) of group Cognitive Behaviour Therapy (CBT)to assist prisoners with symptoms of Traumatic Brain Injury (TBI). |  |
|  | Principal Investigator: | Ms Tracey Mitchell |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 26 January 2017 |  |

Dr Alice Theadom and Dr Elizabeth Du Preez were present in person and Mrs Tracy Mitchell by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The Committee noted the previous decline by the Northern A HDEC and thanked the researcher for their thorough response to the issues raised.

Summary of ethical issues (resolved)

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

1. The Committee noted the high level of vulnerability due to this population being captive. The Researcher(s) stated they are going to ensure contact with their family prior to participation, noting they would assist with costs if necessary to facilitate discussion of participation. The Committee suggested allowing some additional phone time, 20 minutes should be sufficient.
2. The Researcher(s) confirmed all participants have capacity to consent.
3. The Researcher(s) acknowledged this patient population are generally very keen to join any kind of programme whether it is research or not.
4. The Committee urged caution around the view that prisoners wanted to join research for altruistic reasons rather than being an inducement, for a variety of reasons.
5. The Researcher(s) added the CI is more removed from the study overall to combat the potential conflict of interest. As a result from the decline a new means of recruitment has been planned by way of advertisement in the prison, then a member of the healthcare team conducts checking of eligibility.
6. The Committee queried how potential participants could show real interest if they have low literacy, if the advertising was the primary means of recruitment, adding there will be many in this population who have low literacy levels. The Researcher(s) stated information sessions are also available in each health block. The Researcher(s) confirmed psychologist would conduct the information sessions.
7. The Researcher(s) confirmed that it was not possible to conduct this study in another prison to fully mitigate the conflict of interest, due to the unavailability of TBI screening on admission at other prisons.
8. The Committee asked whether prison population moving around is an issue for completing the study. The Researcher(s) stated they will support the participants to stay for the duration of the study, but acknowledged that it is a potential issue. The Researcher(s) noted the sample size has increased that has been allowed for this.
9. The Committee query whether this is same psychologist that report to parole board, and would this be another conflict of interest. The Researcher(s) stated the psychologist will not be involved in parole.
10. The Committee queried the sample size calculations. The Researcher(s) stated a biostatistician calculated them. The Committee accepted the sample size calculation.
11. The Committee suggested AUT could conduct Maori review due to the circumstances that have occurred regarding the prison’s Maori consultation.
12. The Committee confirmed peer review sufficient
13. The Researcher(s) confirmed subsequent offending within system is monitored.
14. The Committee stated the sponsor of this project should be the university.
15. The Researcher(s) confirmed self selected TBI rather than confirmed by medical records.
16. The Committee queried whether there were confidentiality issues if the intern leaves the institution and they had held the key code to link health information. The Researcher(s) explained the lead psychologist that oversees the intern would have access too.
17. The Committee queried how realistic it is for prisoners to access services outlined in the Participant Information Sheet. I.e. mental health services. How quickly if it is not self harm, for instance? The Researcher(s) stated it would be same accessibility as it would outside of study. Triaged process – assessed by nurse. The Researcher(s) confirmed they are not involved in this, unless serious risk of self-harm. Please ensure what is offered is what is available.

Summary of ethical issues (outstanding)

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

1. The Committee asked what the primary outcome was. The Researcher(s) stated it was the concussion symptom Questionnaire. The Committee requested that this was added to the protocol.
2. Reword ad ‘no one will know you’re in it unless you tell them’ – this is naïve, both due to the fact that they are focus groups as well as the fact that people will talk in this patient population.
3. Noted advertising creates an association between cause and effect. I.e. TBI = anger etc. Please review to ensure it does not conflate symptoms with a diagnosis.
4. Please submit CBT protocol.

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

1. Add detail or a consent form for the focus group. Ensure it is clear that they are recorded, who will lead the sessions. The Committee noted most of the questions are actually about the injury for TBI rather than CBT – please make this clear.
2. Add ‘I understand by files will be monitored for change in my behaviour’ in focus group Participant Information Sheet.
3. Add detail on Maori contacts, and who to contact in system to talk to about cultural considerations.
4. Add you will not be advantaged or disadvantaged for participation
5. Add specific information sheet for follow up interview
6. With respect to feedback about the study – this requires CI to be unblinded. The Researcher(s) stated this would occur after the write up. The Committee requested that it is clear that as head of health in this prison will eventually know who took part.
7. Add information about length of time and visits.
8. The Committee query when the waitlist control group monitoring of behaviour starts. The Researcher(s) stated same time as treatment group. The Committee noted it must be very clear that after signing the Participant Information Sheet the participants are effectively being monitored.
9. Remove AUTEC change to HDEC (for ethics review).
10. Make font bigger.
11. Bold and enlarge the heading.
12. The Committee felt Participant Information Sheet was too geared towards a presenting the intervention as treatment. Make it clear this is research and it is randomised.
13. Add health information use, and prison records. That participants have right to see health records while in prison. The Researcher(s) acknowledged this.
14. Add randomisation information.
15. Add that the researchers can help and or support the participants read or with questionaries

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Amend the protocol taking into account the HDECs requirements.
* Amend the advertising for the study.

This following information will be reviewed, and a final decision made on the application, by Dr Nora Lynch and Mrs Kate O Conner.

## Substantial amendments

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| --- | --- | --- | --- |
| **1** | **Ethics ref:** | **NTY/06/07/060/AM06** |  |
|  | Title: | Selenium intake for cancer prevention |  |
|  | Principal Investigator: | Dr. Nishi Karunasinghe |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 26 January 2017 |  |

Dr. Nishi Karunasinghe was present in person for discussion of this amendment.

Potential conflicts of interest

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

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

Summary of Study

1. The Committee and the researchers discussed the history of the research project and the issues encountered by the researchers with regards to extended storage beyond the consented duration and the ethics reporting issues that have occurred.
2. The Committee considered the study’s value as well as taking into account respecting samples and original consents. The Committee noted most of the samples did have consent for future unspecified research.

Summary of ethical issues (outstanding)

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

1. The Committee stated that this study should be closed by way of a final report in this study. A new application should be submitted that considers the study going forward. This application should include detail about the consents given, ability to re-consent and or contact participants and new study objectives and aims.
2. The Committee welcomed the applicants to apply to NTB as they were familiar with the study.
3. Please contact the HDEC Secretariat for assistance with this at [HDECS@moh.govt.nz](mailto:HDECS@moh.govt.nz)

## 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:** | 07 March 2017, 12:00 PM |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

**Problem with Last Minutes**

The minutes of the previous meeting were agreed and signed by the Chair and Co-ordinator as a true record.

The meeting closed at 5.45pm