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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 06 December 2016 |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

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| **Time** | **Item of business** |
| 1.00pm | Welcome |
| 1.05pm  1.30pm | Confirmation of minutes of meeting of 15 November 2016  Review of approved studies (see over for details)  I 13/NTA/100 |
|  | New applications (see over for details) |
| 1.00pm  6.30pm | i 16/NTA/197  ii 16/NTA/199  iii 16/NTA/200  iv 16/NTA/202  v 16/NTA/203  vi 16/NTA/204  vii 16/NTA/205  viii 16/NTA/208  ix 16/NTA/209  x 16/NTA/211  xi 16/NTA/215 |
|  | General business:   * Noting section of agenda |
| 6.30pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Brian Fergus | Lay (consumer/community perspectives) | 11/11/2015 | 11/11/2018 | Present |
| Dr Karen Bartholomew | Non-lay (intervention studies) | 13/05/2016 | 13/05/2019 | Present |
| Dr Christine Crooks | Non-lay (intervention studies) | 11/11/2015 | 11/11/2018 | Present |
| Dr Kate Parker | Non-lay (observational studies) | 11/11/2015 | 11/11/2018 | Apologies |
| Dr Charis Brown | Non-lay (observational studies) | 11/11/2015 | 11/11/2018 | Present |
| Ms Rosemary Abbott | Lay (the law) | 15/03/2016 | 15/03/2019 | Apologies |
| Mrs Leesa Russell | Non-lay (observational studies) | NTB Co-opt | NTB Co-opt | Present |
| Dr Catherine Jackson | Non-lay (health/disability service provision) | 11/11/2016 | 11/11/2019 | Present |
| Ms Toni Millar | Lay (consumer/community perspectives) | 11/11/2016 | 11/11/2019 | Present |
| Dr Angela Ballantyne | Lay (ethical and moral reasoning) | CEN Co-opt | CEN Co-opt | Present |

***Welcome***

The Chair opened the meeting at 1.00pm and welcomed Committee members, noting that apologies had been received from Ms Rosemary Abbott and Dr Kate Parker.

The Chair noted that fewer than five appointed members of the Committee were present, and that it would be necessary to co-opt members of other HDECs in accordance with the SOPs. Dr Angela Ballantyne and Mrs Leesa Russell 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 15 November 2016 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **16/NTA/197** |
|  | Title: | Ketamine and Cognitive Behavioural Therapy for Treatment Resistant Depression |
|  | Principal Investigator: | Ms Ella Kroch |
|  | Sponsor: | Massey University |
|  | Clock Start Date: | 24 November 2016 |

Ms Ella Kroch, Ms Angela McNaught and Mr Rob Sheiff 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. The Researcher(s) explained that despite treatments for major depressive disorder (MDD) advancing considerably in recent years, a significant proportion of patients continue to experience debilitating symptoms after completing several rounds of antidepressants.
2. This population is said to have a form of MDD called treatment resistant depression (TRD), which is considered more disabling than typical MDD and has significant impact on the individual, the health sector, and society.
3. Ketamine is a new treatment for MDD, recently discovered to be a fast acting antidepressant, effective even among patients with TRD. However, despite ketamine’s efficacy and rapid onset, the effects are unfortunately short lived, with improvements only lasting approximately 7 to 18 days.
4. The current pilot study aims to examine whether concurrent Cognitive Behavioural Therapy (CBT) has the potential to extend the effects of Ketamine, and explore the acceptability and feasibility of this combined approach.

Summary of ethical issues (resolved)

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

1. The Committee requested more detail around identifying potential participants as well as determining the capacity to consent, noting the application implied some patients might have limited capacity to consent. The Researcher(s) explained patients would attend a private clinic, as per standard practice. During their first assessment with the consultant psychiatrist the patients would go through their usual assessment and while doing so the psychiatrist would assess whether the patient would meet the inclusion and exclusion criteria, as well as determining capacity to consent. After the assessment, if deemed eligible and competent to give informed consent, the psychiatrist would present all clinical treatment options, including study participation as a potential treatment option. The Participant Information Sheet would be offered, and those interested would take one.
2. The Researcher(s) explained that once the patients had a few days with the Participant Information Sheet they would be contacted by the CI. The CI is not employed by private practice and the patients would be informed that the CI would contact them if they showed interest in the study. If during the call the potential participant were still interested they would be invited to an information session, where family and support people could attend too.
3. The Committee was satisfied with the recruitment procedures.
4. The Committee discussed the potential inducement to participate in the study. This was for two reasons, one was due to the free sessions and the other was simply accessibility to CBT, which can be difficult to access in community contexts. The Researcher(s) explained that in their view the main inducement was perception of optimal treatment, rather than the free sessions. The differential cost will not be a huge factor as many have private medical health insurance. The Committee noted one mitigation would be to not discuss the free sessions when outlining treatment options.
5. The Committee was satisfied that inducements had been addressed.
6. The Committee asked if there would be enough potential participants being referred. The Researcher(s) confirmed most GP referrals to this centre are treatment resistant depression and believed recruitment would not be a problem.
7. The Committee noted the peer review comments. Please explain whether this study will inform a larger trial, or whether it seeks to show whether the treatment is effective. The Researcher(s) explained they are evaluating whether the methodology of her study could be used to determine effectiveness if they did a RCT.

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 whether the CI has expertise to identify participants who are at risk during CBT. Does the CI have adequate support? The Researcher(s) explained there are 3 supervisors’ available and weekly meetings and monitoring. There are also supervisors for all sessions of CBF. The Committee requested these monitoring protections are added to the protocol.
2. The Researcher(s) confirmed participants’ stay on any current treatment for depression throughout the whole study. The Committee requested it is made very clear that there is no need to come off medication to participate, both in the protocol and Participant Information Sheet.
3. The Committee queried why the blood tests (that are mentioned in the protocol) are not in the Participant Information Sheet. The Researcher(s) stated they are clinical tests that occur before participation, and are indications for eligibility. The Committee requested that if they are not done for the study then remove them from the protocol, make it clear they are standard of care, and those results are used to screen for eligibility.
4. The Committee queried what the plan was for the rare but present possibility of a bad ketamine reaction. Please explain the adverse event protocols. The Researcher(s) explained that consultants are always on premises that have access to sedatives etc. The Committee requested a formal plan in the protocol for when things go wrong, who to contact, plan etc. The Committee noted they did not particularly have safety concerns about participant safety but noted how formal protocols reduce risk.
5. The Committee noted the protocol (p.4.2) states CBT can be adapted for participants who identify as Maori. Please add more basic information in the protocol about what changes to the CBT procedures, and added that other participants than those who identify as Maori may benefit from holistic forms of CBT.
6. The Committee asked for the rationale for screening urine for bladder cancer prior to receiving ketamine. The researchers noted that there was a potential risk from ketamine use. The Committee noted that screening for bladder cancer is a potentially problematic clinical issue, and positive tests would need appropriate discussion and follow up, and that as this is not likely to be a risk for a one off dose of ketamine this could be removed. If it is to be maintained as a study procedure it would need substantially more information for management of results in the protocol and explanation in the PIS.

The Committee requested the following changes to the Participant Information Sheet:

1. The Committee noted that while the protocol was clear regarding the doses of study drug and the CBT sessions (i.e. study procedures) the participant information sheet was lacking detail, particularly about what is involved. Please review the protocol against the participant information sheet and include more detail about what is involved if someone chooses to participate. The Committee suggested a table as a means of detailing study procedures.
2. Make it clear that this research is conducted for a PhD qualification
3. Please revise the study documents for clarity, for example the follow up sessions are after the final CBT session. This is not clear at the moment.
4. Remove yes/no for those statements in the consent form that are not truly optional.
5. Add header to the consent form (the same header on the Participant Information Sheet).
6. The Committee noted the side effects for ketamine could last up to 3.5 hours. The Committee noted it was good that the participants would be monitored for the full time, but asked whether participants should be making their own way home afterwards. Please consider adding in the Participant Information Sheet that participants should arrange transport to and from the study visits.

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 the protocol (*Ethical Guidelines for Intervention Studies para* 5.4)

This following information will be reviewed, and a final decision made on the application, by Dr Charis Brown and Dr Fergus.

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| **2** | **Ethics ref:** | **16/NTA/199** |
|  | Title: | Beta-blocker adherence in LQTS |
|  | Principal Investigator: | Dr Kathryn Waddell-Smith |
|  | Sponsor: | ADHB |
|  | Clock Start Date: | 24 November 2016 |

Dr Kathryn Waddell-Smith 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. The Researcher(s) aim to study how adherent people are at taking their medication for their heart condition (long QT syndrome, LQTS) and the reasons behind their adherence or lack thereof.
2. The Researcher(s) plan to administer a brief questionnaire to patients via mail with follow-up either via telephone or at the end of their clinic appointment. They will also collate the required demographic and clinical information from the Cardiac Inherited Disease Registry New Zealand.

Summary of ethical issues (resolved)

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

1. The Researcher(s) confirmed this study was post doctoral and involved a questionnaire administered to adults and children.
2. The Researcher(s) explained potential participants would be identified from Cardiac Inherited Disease registry database.
3. The Committee asked for more information about the registry. The Researcher(s) explained that it was set up in the 1990’s and involves patients referred by GP, cardiologist, paediatricians etc., as well as from coroner when someone dies from a suspected cardiac disease. It involves patients who are at risk of disease, including long QT syndrome. The registry organises screening for patients and their families and help institute risk reducing strategies.
4. The Committee asked what is consented for, in terms of research, when someone signs up to the registry. The Researcher(s) explained patients are told that the registry has two purposes, clinical and research. For research the patient data is used for research (anonymously) and if anything involves a patient or identifiable records they would be contacted about it.
5. The Researcher(s) explained the consent is prospective and the forms mention research. The Researcher(s) had a copy of the consent form. The Committee noted the language on the registry consent form was unhelpfully vague - it did not explicitly state they consented to be either in research (involving their data) or consent to be contacted about 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 asked for clarification around the relationship between this study and a similar HDEC application, referred to in the protocol.
2. The Researcher(s) explained that another researcher was doing very similar research, so they decided to informally link up their projects. The plan was for the other researcher to post a questionnaire. The other study had a broader focus and did not involve children. The application before the Committee today planned to contact those who had long QT syndrome from the other study, as well as contacting those who had children with long QT. The two studies are using some questionnaire tools that are the same, but this study is using more questionnaire tool elements.
3. The Researcher(s) explained that the current plan was to have verbal consent, and the questionnaire to be delivered over the phone.
4. The Committee stated they believed the process for this study should involve a Participant Information Sheet and a consent form, and the questionnaire to be sent out to participants to complete. In terms of the association with the other study, The Committee stated that they should either be totally separate, and this applicant could apply to the HDEC to access some of the other study data as a secondary use request, or the studies should be combined and their inter-relationship clarified.
5. The Committee noted it would likely be easier to keep the studies separate due to this study involving children. The researcher stated that she would like to ask children about their adherence directly, but was unclear as to whether this would be in addition to, or instead of, parental responses. The researcher noted that the children may have different views and this may be a valid research question. The researcher also noted that the questionnaire tools were not designed for children, and it is not clear how appropriate they might be and for what ages. The Committee noted that this needed more thought and clarification and that if research is being conducted with child participants then this required age-appropriate assent forms to empower children to make decisions about themselves and research.
6. The Committee requested a plan to mitigate any risk of distress caused by the questionnaire, as it may raise the fear that participants could suddenly die and were not taking their medication to prevent this. Please include referral plans.
7. The Committee queried the reference to putting in place actions to remove barriers to treatment adherence when identified, as this suggests that the researcher will provide individual level details to treating clinicians which is not what is presented in the application or protocol. The researcher stated that this is not the case.
8. The Committee suggested the registry contact potential participants who could then decide to participate and be sent information about the study.
9. In conclusion, the HDEC had no issues with the goals of the study and felt it had merit and was an important piece of research. The method of recruitment and seeking consent and assent were not up to current ethical standards.

Assent Guidance:

Regarding age groups for different kinds of forms to assist participants under 16 to understand a trial.  
  
**Rules:**  
  
At 16 a person can**consent** to participate. Even so – they may need a very well written information sheet in lay language to understand, and simple language should be used. 

Some children under 16 may be competent to provide **consent**. Most will provide assent, with consent given by legal guardian.

No one can consent on behalf of someone 18 or older to participate in research.   
  
**Guidance:**  
  
When you have participants that are under 16 they need age appropriate written material to help them understand. The age groupings are somewhat irrelevant, as it is a person’s capacity that determines the level of information that should be given to them.  
  
Some children who are under 16 may be competent to provide their own consent.  
  
The best practice for a study involving children and adults would be to have:   
  
An adult (regular) participant information sheet. This is for anyone providing consent. This means it can be used by a participant who is 15 if it is determined that they can understand it.   
  
A shorter, simpler, participant information sheet. This is used for adolescents to provide assent. It would support a verbal discussion about the study. The age range could be 13-15.   
  
A very simple, pictorial, information sheet. This can be 1-2 pages. This is for young participants, for example 7-12.   
  
The age ranges are a guide, they are not rules. The goal is to help participants understand and to determine if they can understand enough to provide consent, or if they are under 16, provide assent (willingness) and their legal guardian consents for them (after being given an ‘adult’ or full information sheet and consent form).

Decision

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

* Please provide age appropriate assent form for non-consenting (children) participants to sign (Ethical Guidelines for Observation Studies 6.21)
* Evidence of free and informed consent by a participant or authorised third party should ordinarily be obtained in writing. (Ethical Guidelines for Observation Studies 6.26)
* 6.29 Some studies may involve interviews or questionnaires that are intrusive and may cause distress. In this case, it is appropriate to seek participants’ prior consent by forewarning them of the potentially distressing nature of participation. (Ethical Guidelines for Observation Studies 6.29)
* All observational studies should be conducted according to written protocols that state the aims of the study, the data needed and how the data will be collected, used and protected. Currently the protocol refers to another ethics application and study. Please separate these studies (Ethical Guidelines for Observation Studies 5.11)
* The Committee suggest that the researcher rewrites their Protocol to reflect how they might well approach the project in light of the Committee’s comments, and then align all subsequent documents to the Protocol. As noted earlier, the Committee is supportive of what they are trying to achieve but it is important to have the correct approach.

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| **3** | **Ethics ref:** | **16/NTA/200** |
|  | Title: | Whānau Pakari on Orimupiko marae |
|  | Principal Investigator: | Dr Yvonne Anderson |
|  | Sponsor: | University of Auckland |
|  | Clock Start Date: | 24 November 2016 |

Dr Yvonne Anderson and Ms Cervantes Wild were present 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. Whānau Pakari is a novel multi-disciplinary intervention programme for obese children and adolescents in Taranaki.
2. A randomised clinical trial was undertaken to assess outcome (CEN/11/09/054). This showed that both an intense weekly 12-month intervention programme and a less intense 6-month assessment approach achieved clinically meaningful and significant reductions in body mass index.
3. Those that attended >70% of sessions achieved greater BMI SDS reductions, however Māori retention rates were lower than those of non-Māori , and Māori did not achieve the same BMISDS reduction as New Zealand European participants.
4. Whānau Pakari achieved a high recruitment rate from Māori into the programme (45%, which is equal to that of NZ European participants). If retention could be improved for Māori, ethnic disparities in outcome may be eliminated.
5. To address this, a marae based pilot of a wider programme informed by Whānau Pakari principles with increased leadership by Māori is proposed, as requested by a local whānau.
6. This programme will enable and support whānau to take ownership of their long-term health and wellbeing. The project is innovative and there is a genuine partnership relationship between Western science and Māori knowledge at multiple levels, from programme delivery to senior advisors. It is anticipated that with this model, there will be a significant BMI SDS reduction over a 12-month period.
7. The Committee is supportive of these efforts by the researcher to address health inequalities.

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 a justification for paying child participants for blood tests. The Researcher(s) explained that motivation to continue regular blood tests could be difficult to maintain. This was experienced in prior studies. Ethics approved vouchers for blood tests in the prior studies, and The Researcher(s) sought to do the same in this study. The Committee accepted the amount given was not considered an unjust inducement.
2. The Researcher(s) explained this study also assess if the location of the intervention was a relevant factor.
3. The Researcher(s) noted rural Maori were not represented same as other groups. The Researcher(s) were not sure of the prevalence of obesity in this group but fairly sure there is a health problem.
4. In terms of other differences from the current intervention, apart from shifting the intervention location to the Marae, this study involves a lot more consultation at front end by Iwi themselves and higher degree of whanau involvement. This study is also more about transition of ownership of the research and results to get sustained benefits from the research.
5. The Committee asked who makes referrals. The Researcher(s) stated anyone can, explaining that in prior study they widened the referral base so there were no barriers.
6. The Committee asked for a response to the peer review comments, in particular about the design and methods. The Researcher(s) explained the urban group is not an informal control group. As far as it being a proxy control – this was not intended. The Researcher(s) are looking at pre and post intervention results to see if potential of health delivery on the Marae in a more structured way is beneficial.

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 for clarification around who were considered the participant in this project. The Researcher(s) confirmed the child is the index participant and the family were linked, or extended links, but the children were the focus.
2. The Researcher(s) added if recruitment were low they would consider opening it up to adults too.
3. The Committee noted the importance of figuring out who the participants were, in order to know what the child consents for, for themselves, what parents’ consent for, for their children, and what adults consent for, for themselves. This might be most clearly set out with three participant information sheets with specific procedures for each participant group.
4. The Researcher(s) added there is a commitment contract that would, in most settings, be signed on behalf of the whanau, one by a member on behalf of child, and one for themselves (as an adult). The Committee noted that if this is a programme that is being delivered and then evaluated it is different from research. If this is a research project then the Committee requires ethical standards for research to be met, which involves Participant Information Sheet and Assent forms, and a clear research protocol.
5. Please use Statistics New Zealand's ethnicity classifications when collecting ethnicity data to ensure the options available are suitable for New Zealand participants. These classifications are: New Zealand European, Maori, Samoan, Cook Islands Maori, Tongan, Niuean, Chinese, Indian, Other (such as Dutch, Japanese, Tokelauan). For more information see <http://www.health.govt.nz/publication/ethnicity-data-protocols-health-and-disability-sector>.
6. The Committee requested three participant Information Sheets to cover children, adults consenting on behalf of children and adults as participants. The Committee requested assent forms of children who can’t provide their own consent.

Assent Guidance:

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The best practice for a study involving children and adults would be to have:   
  
An adult (regular) participant information sheet. This is for anyone providing consent. This means it can be used by a participant who is 15 if it is determined that they can understand it.   
  
A shorter, simpler, participant information sheet. This is used for adolescents to provide assent. It would support a verbal discussion about the study. The age range could be 13-15.   
  
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The age ranges are a guide, they are not rules. The goal is to help participants understand and to determine if they can understand enough to provide consent, or if they are under 16, provide assent (willingness) and their legal guardian consents for them (after being given an ‘adult’ or full information sheet and consent form).

The Committee requested the following changes to the Participant Information Sheet:

1. Nothing in current Participant Information Sheet states information will be sought from GPs. If you do plan to seek GP data then this needs to be clearly explained in the Participant Information Sheet.
2. Similarly, there should be information on return of incidental findings or risks from study related screening (from blood tests for example) and consent for where these results go (i.e. back to GP). This is particularly important if these people are not presently engaging with primary care.
3. The Researcher(s) stated all participants will have a GP, it is just that they do not go to their GP visits. The Committee asked if it is a requirement to participate that they have a GP. The Researcher(s) confirmed it was, due to need for clinical referral in event of co-morbidity findings. Please add this information to the Participant Information Sheet
4. Be clear what blood tests are about and what is being tested.
5. The ACC statement should state: 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.
6. Clarify the follow up for participants and if it is dependent upon funding explain this, as their participation may last 5 years.
7. The Committee explained that information around who will access their data must be clarified in the Participant Information Sheet, of particular importance is any identifiable information.
8. Be clear about PhD student involvement (if that occurs).
9. Review for jargon and explain in lay language.
10. Add all logos of involved organisations.

Decision

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

* Please provide age appropriate assent form for non-consenting (children) participants to sign (Ethical Guidelines for Observation Studies 6.21)
* 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 Karen Bartholomew and Mrs Toni Millar.

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| **4** | **Ethics ref:** | **16/NTA/202** |
|  | Title: | GSK ASCEND-D 200807 |
|  | Principal Investigator: | Dr Kannaiyan Rabindranath |
|  | Sponsor: | PPD |
|  | Clock Start Date: | 24 November 2016 |

Dr Kannaiyan Rabindranath 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 randomized, open-label (sponsor-blind), active controlled, parallel-group, multi-center, event driven study in dialysis subjects with anemia associated with chronic kidney disease to evaluate the safety and efficacy of daprodustat compared to recombinant human erythropoietin, following a switch from erythropoietin-stimulating agents.

Summary of ethical issues (resolved)

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

1. The Researcher(s) explained the rationale for the study (finding an oral treatment compared to injections). The Committee requested this information is added to the opening paragraph.
2. The Committee asked for clarification around the length of the trial. The Researcher(s) confirmed there was a total of four years, with monthly visits for the first year.
3. The Committee asked about the recruitment strategy for the study. The Researcher(s) explained they identify potential participants from records. The study co-ordinator makes contact and asks whether they are interested in participating. If interested a Participant Information Sheet is sent out. The potential participant comes into clinic and meets the CI, who will go through the study with them. The Committee noted they prefer a clinician to make first contact, as to avoid records being accessed by researchers. The Researcher(s) stated that these patients are well known by the co-ordinators.
4. The Committee noted a number of ethics application questions were poorly completed. In particular, those relating to the ethical issues in the study, benefit to Maori and the use of human tissue.
5. The Researcher(s) explained the prevalence in Maori, in particular the relationship to diabetes.

Summary of ethical issues (outstanding)

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

1. Please clarify if the study doctor is paid directly.
2. The Committee noted that it is not acceptable for the study to be stopped for commercial reasons. Please remove any mention of stopping the trial for such reasons. The Researcher noted they were not concerned for the patients if this happens as the standard of care treatment has same efficacy. The value of this trial is that daprodusat can be administered orally rather than as an infusion which will be beneficial for the patient
3. The Committee noted GSK and the sponsor couldn’t have any access to personal information or identifiable health records.
4. The Researcher(s) explained how drug re-starts after liver failure occurs.
5. The Researcher(s) explained why they are running the site as the lead site and their other trial experience. The Committee was satisfied with the CI’s experience.

The Committee requested the following changes to the Participant Information Sheet:

1. The Committee requested that the study re-start drug was a stand-alone document, and should not refer to the original Participant Information Sheet.
2. Device malfunction on Pg. 8 – please clarify what this means.
3. On page 13 of 18. Under data protection law. ‘in order to protect’….states that the study is blinded. This study is not blinded to participants. Please revise.
4. Remove witness statements on the consent form.
5. Risk information is inadequate. Please quantify the risks. In both PIS, particularly in the restart drug after event – as serious illness/death was mentioned twice.
6. Participant Information Sheet has lack of study procedures. Please revise and add missing procedures.
7. The Committee requested a table to outline study procedures and visits for participants.
8. Revise and remove any US references and replace with New Zealand language or references. IRB etc.
9. Identifiable records **cannot** go to the sponsor. Remove any mention of this from the Participant Information Sheet And CF.
10. Remove verbal consent (consent form).
11. Make dosing clear – in particular that dosage varies on outcomes of a blood test.
12. Blood work information is understated. Please add more information on the tests that will occur.
13. The optional future unspecified research Participant Information Sheet requires the below to be included as per the Ministry of Health Guidelines.

Please ensure all of the following are included in the future unspecified research forms:

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| * An indication of the type and nature of the research to be carried out and its implications for the donor, where possible, and an explanation of why the potential donor is being approached for their tissue and specifically what tissue is being sought. |
| * Known possible researchers or institutions that might use the tissue sample, if possible. |
| * Whether the donor’s sample is going to be, or is likely to be sent overseas, and where possible, to what country or countries. |
| * Acknowledgement that all future unspecified research in New Zealand will be subject to ethical review. However, when a tissue sample is sent overseas, unless it is sent in conjunction with a New Zealand research project, future research is likely to be considered by an overseas ethics committee without New Zealand representation. |
| * Whether the donor’s identity and details will remain linked with the sample or whether the sample will be de-linked. |
| * A statement that if a donor consents to a tissue sample being unidentified or de-linked, they relinquish their right to withdraw consent in the future. |
| * Whether the donor may be contacted in the future regarding their tissue sample. Whether or not, and under what circumstances, information about the future unspecified research will be made available to the donor and/or (where relevant) their clinician. |
| * Acknowledgement that the donor will not own any intellectual property that may arise from any future research. |
| * Whether there is provision to withdraw consent for the use of human tissue samples in the future. Where there is provision to withdraw consent, only tissue samples remaining at the time of a request to withdraw and any information held for future unspecified research may practically be withdrawn. Tissue samples or information used in research before the request to withdraw is received is unlikely to be able to be returned or destroyed. |
| * Acknowledgement that the donor’s decision regarding the consent for use of their tissue sample for unspecified future research will in no way affect the quality of a donor’s current or future clinical care. |
| * Where and for how long a tissue sample will be stored, how it will be disposed of and whether there is a cultural protocol for its disposal. For example, information about the institution holding the tissue sample: its aims, research procedures and research governance. |
| * Whether or not tissue samples could be provided to other researchers and institutions, and whether or not such provision could include sending samples to other countries |
| * Whether or not collected samples will be provided to commercial biomedical companies or will be used in commercial research collaborations, if known. |
| * What provisions will be made to ensure patient confidentiality. |
| * That different cultural views may inform choice about donation of tissue; for example, for some Maori, human tissue contains genetic material that is considered to be collectively owned by whanau, hapu and iwi. |
| * That cultural concerns may arise when tissue samples are sent overseas, including how tissue samples are stored and disposed of. Processes for monitoring and tracking what happens to samples may not be acceptable to donors. |
| * That donors may want to discuss the issue of donation with those close to them, for example; family, whanau, hapu and iwi. |

Decision

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

* Please ensure Participant Information Sheet and Consent Form for the use of tissue for future unspecified research includes all requirements (*Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes, para 2*).
* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Please provide criteria for study termination. (*Ethical Guidelines for Intervention Studies* *para 6.64*).
* Explain what happens to health information (*Ethical Guidelines for Intervention Studies* *para 7.7)*
* Please see (*Ethical Guidelines for Intervention Studies para* 7.2) for more information on levels of data confidentiality.

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

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| **5** | **Ethics ref:** | **16/NTA/203** |
|  | Title: | GSK ASCEND-ND 200808 |
|  | Principal Investigator: | Dr Kannaiyan Rabindranath |
|  | Sponsor: | PPD |
|  | Clock Start Date: | 24 November 2016 |

Dr Kannaiyan Rabindranath 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 randomized, open-label (sponsor-blind), active controlled,

parallel-group, multi-center, event driven study in non-dialysis subjects with anemia associated with chronic kidney disease to evaluate the safety and efficacy of daprodustat compared to darbepoetin alfa.

Summary of ethical issues (resolved)

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

1. The Researcher(s) explained the rationale for the study (finding an oral treatment compared to injections). The Committee requested this information is added to the opening paragraph.
2. The Committee asked for clarification around the length of the trial. The Researcher(s) confirmed there was a total of four years, with monthly visits for the first year.
3. The Committee asked about the recruitment strategy for the study. The Researcher(s) explained they identify potential participants from records. The study co-ordinator makes contact and asks whether they are interested in participating. If interested a Participant Information Sheet is sent out. The potential participant comes into clinic and meets the CI, who will go through the study with them. The Committee noted they prefer a clinician to make first contact, as to avoid records being accessed by researchers. The Researcher(s) stated that these patients are well known by the co-ordinators.
4. The Committee noted a number of ethics application questions were poorly completed. In particular, those relating to the ethical issues in the study, benefit to Maori and the use of human tissue.
5. The Researcher(s) explained the prevalence in Maori, in particular the relationship to diabetes.

Summary of ethical issues (outstanding)

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

1. The Committee noted that it is not acceptable for the study to be stopped for commercial reasons. Please remove any mention of stopping the trial for such reasons. The Committee noted that it is not acceptable for the study to be stopped for commercial reasons. Please remove any mention of stopping the trial for such reasons. The Researcher noted they were not concerned for the patients if this happens as the standard of care treatment has same efficacy. The value of this trial is that daprodusat can be administered orally rather than as an infusion which will be beneficial for the patient
2. The Committee noted GSK and the sponsor couldn’t have any access to personal information or identifiable health records.
3. The Researcher(s) explained how drug re-starts after liver failure occurs.
4. The Researcher(s) explained why they are running the site as the lead site and their other trial experience. The Committee was satisfied with the CI’s experience.

The Committee requested the following changes to the Participant Information Sheet:

1. The Committee requested that the study re-start drug was a stand-alone document, and should not refer to the original Participant Information Sheet.
2. Device malfunction on Pg. 8 – please clarify what this means.
3. On page 13 of 18. Under data protection law. ‘in order to protect’….states that the study is blinded. This study is not blinded to participants. Please revise.
4. Remove witness statements on the consent form.
5. Risk information is inadequate. Please quantify the risks. In both PIS, particularly in the restart drug after event – as serious illness/death was mentioned twice.
6. Participant Information Sheet has lack of study procedures. Please revise and add missing procedures.
7. The Committee requested a table to outline study procedures and visits for participants.
8. Revise and remove any US references and replace with New Zealand language or references. IRB etc.
9. Identifiable records **cannot** go to the sponsor. Remove any mention of this from the Participant Information Sheet.
10. Remove verbal consent (consent form).
11. Make dosing clear – in particular that dosage varies on outcomes of a blood test.
12. Blood work information is very understated. Please add more information on the tests that will occur.
13. The optional future unspecified research Participant Information Sheet requires the below to be included.

Please ensure all of the following are included in the future unspecified research forms:

|  |
| --- |
| * An indication of the type and nature of the research to be carried out and its implications for the donor, where possible, and an explanation of why the potential donor is being approached for their tissue and specifically what tissue is being sought. |
| * Known possible researchers or institutions that might use the tissue sample, if possible. |
| * Whether the donor’s sample is going to be, or is likely to be sent overseas, and where possible, to what country or countries. |
| * Acknowledgement that all future unspecified research in New Zealand will be subject to ethical review. However, when a tissue sample is sent overseas, unless it is sent in conjunction with a New Zealand research project, future research is likely to be considered by an overseas ethics committee without New Zealand representation. |
| * Whether the donor’s identity and details will remain linked with the sample or whether the sample will be de-linked. |
| * A statement that if a donor consents to a tissue sample being unidentified or de-linked, they relinquish their right to withdraw consent in the future. |
| * Whether the donor may be contacted in the future regarding their tissue sample. Whether or not, and under what circumstances, information about the future unspecified research will be made available to the donor and/or (where relevant) their clinician. |
| * Acknowledgement that the donor will not own any intellectual property that may arise from any future research. |
| * Whether there is provision to withdraw consent for the use of human tissue samples in the future. Where there is provision to withdraw consent, only tissue samples remaining at the time of a request to withdraw and any information held for future unspecified research may practically be withdrawn. Tissue samples or information used in research before the request to withdraw is received is unlikely to be able to be returned or destroyed. |
| * Acknowledgement that the donor’s decision regarding the consent for use of their tissue sample for unspecified future research will in no way affect the quality of a donor’s current or future clinical care. |
| * Where and for how long a tissue sample will be stored, how it will be disposed of and whether there is a cultural protocol for its disposal. For example, information about the institution holding the tissue sample: its aims, research procedures and research governance. |
| * Whether or not tissue samples could be provided to other researchers and institutions, and whether or not such provision could include sending samples to other countries |
| * Whether or not collected samples will be provided to commercial biomedical companies or will be used in commercial research collaborations, if known. |
| * What provisions will be made to ensure patient confidentiality. |
| * That different cultural views may inform choice about donation of tissue; for example, for some Maori, human tissue contains genetic material that is considered to be collectively owned by whanau, hapu and iwi. |
| * That cultural concerns may arise when tissue samples are sent overseas, including how tissue samples are stored and disposed of. Processes for monitoring and tracking what happens to samples may not be acceptable to donors. |
| * That donors may want to discuss the issue of donation with those close to them, for example; family, whanau, hapu and iwi. |

Decision

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

* Please ensure Participant Information Sheet and Consent Form for the use of tissue for future unspecified research includes all requirements (*Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes, para 2*).
* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Please provide criteria for study termination. (*Ethical Guidelines for Intervention Studies* *para 6.64*).
* Explain what happens to health information (*Ethical Guidelines for Intervention Studies* *para 7.7)*
* Please see (*Ethical Guidelines for Intervention Studies para* 7.2) for more information on levels of data confidentiality.

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

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| **6** | **Ethics ref:** | **16/NTA/204** |
|  | Title: | The Attain Study |
|  | Principal Investigator: | Dr Kate Gardner |
|  | Sponsor: | Covance New Zealand Ltd |
|  | Clock Start Date: | 24 November 2016 |

Dr Kate Gardner 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.

Dr Christine Crooks declared a potential conflict of interest, and the Committee decided the member would stay in room but not participate in discussion or decision for the application.

Summary of Study

1. This is an open-label, randomized, two-group, multicenter, international Phase 3 study of NKTR-102 versus TPC in patients with breast cancer brain metastases (BCBM) who have stable brain metastases and have been previously treated with an anthracycline, ataxane, and capecitabine in either the adjuvant or metastatic setting.
2. This study will randomize approximately 350 patients using a 1:1 randomization ratio and stratification based on geographic region, tumour receptor status, and Eastern Cooperative Oncology Group (ECOG) status. At Screening, the Investigator must determine which TPC will be offered to the patient.
3. An independent data monitoring committee (DMC) will assess interim safety and efficacy data.

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 applicant noted these potential participants are vulnerable but this is not expressed in the application. Please explain how this group (people with terminal illness) are interacted with sensitively, with reference to New Zealand ethics guidelines.
2. The Committee noted there is a need for drugs that treat diarrhoea – please explain where these support drugs coming from, whether they are free of charge, and explain when the medication is provided. The Committee expects the drugs to be given before the participants experience symptoms.
3. Please clarify the process for screening (generally). R.2.1.1 indicates there is a screening log.
4. P.4.1 – notes the prevalence in Maori but there is no analysis of ethnicity in the study protocol. The Committee notes the small sample size and asked if this is the reason for a lack of ethnic analysis.
5. Page 3 of PK sub-study states the link code is stored ‘at your doctor’s office’. This is not correct, the participant’s regular doctor will not hold this link? Please explain to HDEC and update the participant information sheet with correct information.
6. Please explain for Future Unspecified Research how the notification of new research studies and right to refuse them (for samples going overseas) works for participants. Page 2 of future unspecified research participant information sheet. This would require sophisticated notification and consenting systems.

The Committee requested the following changes to the Participant Information Sheet:

1. What does too much of any drug mean in this context? Provide more clarity.
2. Please review for jargon and explain terms in lay language (across all participant information sheets).
3. Be specific about where samples are stored (country).
4. No length of time for storage or genetic testing information. Please add more information for participants.
5. Remove cross referencing between the future unspecified research, PK sub study and main participant information sheet. They must be standalone documents.
6. Query study termination criteria – not for commercial reasons. What are other reasons?
7. Page 16 implies that participants can choose identified or linked data for Future Unspecified Research. The Committee noted that no identifiable records should be sent to the sponsor, particularly when linked to samples, - only de-identified. Remove this wording.
8. The PK sampling participant information sheet contains sentences that are far too broad and resemble future unspecified research. Please limit the document to only cover optional additional PK sampling, and conduct broader future unspecified research in the future unspecified research document.
9. The current optional participant information sheets are missing crucial information, outlined in the Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes 2007. Please review the guidelines and ensure all information is included. There is further guidance at <http://ethics.health.govt.nz/> under quick links, features of informed consent.

Decision

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

* Please ensure the separate Participant Information Sheet and Consent Form for the use of tissue for future unspecified research cover all requirements (*Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes, para 2*).
* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Explain what happens to health information, noting the concerns raised by the Committee (*Ethical Guidelines for Intervention Studies* *para 7.7)*
* Provide further information on the study design, *in particular* how and when side effects are managed with supplementary drugs (*Ethical Guidelines for Intervention Studies para* 5.4)
* Provide details on what processes are in place to accommodate the highly vulnerable context of recruitment *(Ethical Guidelines for Intervention Studies para 6.2).*

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

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| **7** | **Ethics ref:** | **16/NTA/205** |
|  | Title: | (duplicate) Antibiotic Timing and Culture Yields in Paediatric Musculoskeletal Infection |
|  | Principal Investigator: | Mr Matthew Boyle |
|  | Sponsor: |  |
|  | Clock Start Date: | 24 November 2016 |

Mr Matthew Boyle 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 was resubmission of an earlier application declined by Northern B
2. The presence of the researcher greatly assisted the Committee in explaining some details to their satisfaction
3. The Researcher(s) confirmed there was no need for linking data.
4. The Committee asked about the database referenced in the application. The Researcher(s) explained it was a retrospective audit.
5. The Committee noted the response to the decline letter from the previous committee and stated all requirements had been addressed.

Decision

This application was *approved* by consensus.

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| **8** | **Ethics ref:** | **16/NTA/208** |
|  | Title: | The CREEDS Study |
|  | Principal Investigator: | Assoc. Prof Jeremy Krebs |
|  | Sponsor: |  |
|  | Clock Start Date: | 18 November 2016 |

Dr Brian Corley and co-investigators were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The study is an investigation of the effects of two different kinds of caloric restriction on resting energy expenditure.
2. Participants will be randomized in a 1:1 to ratio to a calorie-restricted diet of 80% of predicted requirements versus a very low calorie intermittent caloric restriction, 25% of requirements for 2 days per week for 6 weeks.
3. Body composition by DEXA scan, energy expenditure by indirect calorimetry, height weight, hunger, physical activity and diet composition will all be recorded. Blood tests looking at hormones involved in adaptive thermogenesis will be collected also.

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 about the return of samples plan. The Researcher(s) explained samples are stored in tissue bank who have a safe and well managed return of samples process. Participants can liaise with the bank, who use couriers.
2. The Researchers confirmed that the diet is prescribed and will cost the same and certainly not more than what participants are already paying to eat.
3. The Researchers confirmed they provide food for participants on the fasted study visits.
4. The Committee asked how compliance is managed. The Researcher stated the participants are contacted on regular basis, adding there is scope for adjusting food or provide strategies to try and address challenges experienced by participants, particularly for fasting days.
5. The Committee queried the sample size. The Researcher explained it is based on existing studies that have closely resembled studies like ours. The Researchers acknowledged there are differences between the studies, however there is a currently running pilot study that will better refine the power of the study. The Committee noted any changes to sample size will require submission to HDEC as an amendment.
6. The Committee queried the peer review feedback on ethnicity. The Researcher(s) state design was well received but acknowledged that they will meet with peer reviewer and look at scope for us to do additional analysis.
7. The Committee asked about the inclusion exclusion criteria, noting the study excluded females but had a wide age range and included any ethnicity. The Committee asked whether there are interethnic variations that would pose issues with analysis. The researcher stated there no substantial evidence to suggest that ethnicity would be a compounder for body composition. In response to the exclusion of women, the Researcher(s) explained the need to only have men is due to the unpredictable menstrual cycle and how that impacts energy expenditure.
8. The Researcher(s) explained that it would be clearest to demonstrate the study hypothesis in men. The Committee noted ethics guidelines state that it is only ever justifiable to exclude a group if it fundamental to the study. Being difficult to conduct the study is not a justification.
9. The Researcher(s) explained that making the results valid depends on how that energy restriction function occurs in relation to change in menstrual cycle. It would require daily monitoring during menstrual cycles, which is not feasible for this study.
10. The Committee accepted exclusion of women on the groups that this study question could not be answered for women in this application.
11. The Researcher explained the recruitment process.
12. The Committee asked why samples were being stored. The Researcher(s) stated to answer questions around adaptive thermogenesis, hormones and body fat and body composition levels.

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 participant information sheet for future unspecified research states ‘Results are sent to file addresses. The Committee asked what kind of results this refers to, study results, personal results etc. Please clarify.

The Committee requested the following changes to the Participant Information Sheet:

1. Confidentiality – please expand what is in ‘policy’ as participants won’t know what this entails.
2. Add inclusion exclusion criteria to Participant Information Sheet
3. Add to procedures section in Participant Information Sheet the intention to contact GPs about adverse results as well as for medical history.
4. The Committee ask why participants have to fill 3 food diaries, asking what it used for. The Researcher(s) stated it is for quality and compliance for primary analysis. Add Participant Information Sheet that this is an assessment of compliance.
5. Add justification and explanation around why samples might be stored for future unspecified research.

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*).
* Explain what happens to health information, in particular to the ‘results’ from future unspecified research (*Ethical Guidelines for Intervention Studies* *para 7.7).*

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

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| **9** | **Ethics ref:** | **16/NTA/209** |
|  | Title: | NIMO-Prem |
|  | Principal Investigator: | Dr Maria Saito Benz |
|  | Sponsor: | Capital and Coast District Health Board |
|  | Clock Start Date: | 24 November 2016 |

Dr Maria Saito Benz 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. One in 12 babies in New Zealand are born premature. Premature infants, especially those born less than 30 weeks gestation and/or extremely low birth weight (<1000g), carry a disproportionate burden of mortality and lifelong neurodevelopmental disability when compared to their healthy term-born peers.
2. For healthy brain development ensuring adequate supply of oxygenated blood to the brain is critical; however, what constitutes the 'optimal' brain perfusion and oxygen level in premature infants is currently unknown.
3. In this observational study we will utilise portable and non-invasive equipment and radiological imaging to develop better understanding of the optimal brain perfusion and oxygenation targets to prevent mortality and later neurodevelopmental disability.

Summary of ethical issues (resolved)

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

1. The Researcher(s) explained the fragile nature of the baby. The Researcher(s) explained that handling is kept to a minimum, and when more intensive observations occur, for example MRI scans, and it is later on once the babies are more robust.
2. The Researchers confirmed MRI and additional scans are not standards of care, adding the 12-24 months neurodevelopment follow up are also additional to standard of care.
3. The Committee note the two consent forms, prospective and retrospective.
4. The Researcher explained that there are usually long discussions around the patient’s clinical care in cases of expected premature babies. The patients are approached as early as possible to give them time to consider participation. However, there will be a group of babies who will be born under urgency with no chance of prospective consent. The Researchers stated this group will be small, but clinically important, adding they also have a right to participate in research.
5. The Committee was happy with the prospectively enrolled research project and noted its importance, and noted the monitoring was low risk.
6. The Committee noted there needs to be a full consideration of the legal implications of enrolling a newborn into observational research without the consent of the mother. This part of the study should be heard separately as an amendment to the study. The Committee noted this is not an ethical issue it’s a legal issue. Ethically, the Committee felt the enrolment of babies into the study was well founded due to the minimal risk, the benefits of more monitoring and the public value of the study. Further consideration could be given regarding consent of the other parent even around the time of delivery, it does not have to be maternal consent.
7. HDECs can consider your study ethically, but cannot approve the non-consensual aspect if you do not make a case with regards to the legal requirements below:  
     
   Right 7.4 of the HDC Code of Rights states that “Where a consumer is not competent to make an informed choice and give informed consent, and no person entitled to consent on behalf of the consumer is available, the provider may provide services where –   
    a) It is in the best interests of the consumer; and   
   b) Reasonable steps have been taken to ascertain the views of the consumer; and   
   c) Either, -   
    i. If the consumer's views have been ascertained, and having regard to those views, the provider believes, on reasonable grounds, that the provision of the services is consistent with the informed choice the consumer would make if he or she were competent; or   
    ii. If the consumer's views have not been ascertained, the provider takes into account the views of other suitable persons who are interested in the welfare of the consumer and available to advise the provider.”   
     
   Right 9 ensures that these rights extend to those occasions when a consumer is participating in, or it is proposed that a consumer participate in, teaching or research.   
     
   It is possible to approve a study (under Right 7.4) if it can be shown that participation is in the best interest of the consumer and they take into account the views of other suitable persons or believe that the consumer would wish to consent if they were able to. In these cases the consent can be provided by the clinician for this individual to participate in the research.
8. The Committee note participation in the research as a whole could be in best interest due to increased follow up and data to monitor clinical decision making.
9. We suggest that the legal advisers to the DHB address this matter and express an opinion

Summary of ethical issues (outstanding)

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

1. Add document that outlines screening process, or add to the protocol.

The Committee requested the following changes to the Participant Information Sheet:

1. Please provide a plan for statistical analysis.
2. Amend to ‘tests pose no risk’ – not equipment pose no risk.
3. Add the below to the ACC statement:

If you were injured in this study, which is unlikely, you would be eligible **to apply** for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery.  
  
If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.

1. Add that this study is part of a PhD project.

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*).
* Should you wish this decision include the retrospective arm then we would require you to supply documentation that you have sought legal advice, and if you have, also supply amended Information Sheet and Consent Form appropriately worded.

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

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| **10** | **Ethics ref:** | **16/NTA/211** |
|  | Title: | Experiences of prescription and over-the-counter opioid dependence |
|  | Principal Investigator: | Ms Carina Walters |
|  | Sponsor: | The University of Auckland |
|  | Clock Start Date: | 24 November 2016 |

Ms Carina Walters 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 longitudinal qualitative design, and aims to describe the experiences of people who develop pharmaceutical opioid dependence through non-illicit pathways.
2. Study objectives are: to describe the experiences and health, dependence and quality of life outcomes of people who are entering treatment for pharmaceutical opioid dependence over a 6 month period, and to describe the same parameters for people with pharmaceutical opioid dependence who are not accessing treatment over a 6 month period.
3. Participants will be recruited via advertisement in a treatment service for opioid dependence (CADS), and via flyers in GP waiting rooms, community pharmacies and the University of Auckland Facebook account.
4. If insufficient participants are reached through these methods, a publicity release will be prepared describing the key issues of pharmaceutical opioid dependence and the aims of the study, and giving contact details for interested parties, which may be reported by media.
5. A study website will also be developed to provide detailed information about the study to interested parties. One hour interviews will be conducted at three time points (entry to the study, 3 months post entry and 6 months post entry). Analysis will be performed using a general inductive approach, and framework analysis, and aims to compare groups and individuals across time.

Summary of ethical issues (resolved)

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

1. The Researcher(s) explained that they have a fairly good idea about how people develop illicit addictions and how treatment works for them. However how addiction develops and treatment works for people who developed addiction through non illicit drugs is less evidence based.
2. The Committee queried how the researchers manage whether people have capacity to participate (are able to consent). The Researcher(s) explained brochures will be in CADDS and pharmacies but no active recruitment. Participants will only ever volunteer themselves. Family involvement and time to consider participation are both further mitigation strategies.
3. The Researcher explained, once a potential participant makes contact the researcher’s conducts some basic screening. If interested they are sent more information, followed by an in person consent procedure.
4. The Committee asked whether the researchers will screen for risks, i.e. depression. The Researcher(s) noted axis one disorders are not excluded as they will be a co-morbidity for many of these potential participants, but they will refer for support if someone raises concerns during the study. Could all participants be offered support information eg helpline numbers.
5. The Committee asked what happens to data from screening for those who turn out not to be eligible? The Researcher stated it would be destroyed.
6. The Researcher(s) explained they have an advisor for Maori for study, felt important to collect same ethnicity as census questions. The Researcher explained that the analysis is qualitative (per individual) however if there are any notable differences between ethnicities experience they will be reported and explored.
7. Please use Statistics New Zealand's ethnicity classifications when collecting ethnicity data to ensure the options available are suitable for New Zealand participants. These classifications are: New Zealand European, Maori, Samoan, Cook Islands Maori, Tongan, Niuean, Chinese, Indian, Other (such as Dutch, Japanese, Tokelauan). For more information see <http://www.health.govt.nz/publication/ethnicity-data-protocols-health-and-disability-sector>.
8. The Committee asked why there were so many formal re-consenting procedures. The Researcher(s) stated that in longitudinal studies it is good to keep re-consenting. The Committee noted it is sufficient to check if they happy to continue to participate but no need to formally re-consent.
9. The Committee discussed the vulnerability of the groups. Will refer to provider if not on treatment? The Researcher(s) explained yes they would use diagnostic manual, determine likely to be dependent (or not) and if so will provide treatment options.
10. The Researcher(s) confirmed screening failures get treatment options too.
11. The Researcher(s) stated will add flyer on Auckland university website. One for community population in pharmacy.
12. Please ensure people self-select to participate – the pharmacists should not recruit.

Summary of ethical issues (outstanding)

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

1. Provide procedures around advertising on social media. Ensure the ad can’t be shared or commented on.
2. Safety information – add safety plan to the protocol and potentially some information in the participant information sheet. This relates to both safety for researchers (safety while interviewing) and for participants. Two elements, psychological risk/distress mitigation and referral approaches / standard information to give if incidental findings, mental health issues or suicidality are identified.
3. The Committee asked whether it is valid to conduct outcome measures in an untreated population. The Researcher(s) noted intra-participant comparison rather than comparing the groups as a whole.
4. Add in protocol comparisons / over time outcome comparison.

The Committee requested the following changes to the Participant Information Sheet:

1. In Participant Information Sheet does not explain study is comparing outcomes (this is deception as it stands). Please explain how comparisons will occur or at least that there are two groups.
2. Make clear this is for the completion of a PhD.
3. Participant Information Sheet – add all procedures (i.e. questionnaires etc.)
4. Make limits of confidentiality in the Participant Information Sheet not just on the consent form.

Decision

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

* Please amend the information sheet and consent 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 comparison analysis and advertising safety measures* (*Ethical Guidelines for Intervention Studies para* 5.4)

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

|  |  |  |
| --- | --- | --- |
| **11** | **Ethics ref:** | **16/NTA/215** |
|  | Title: | Emergency treatment of anterior shoulder dislocations |
|  | Principal Investigator: | Dr. Mark Sagarin |
|  | Sponsor: |  |
|  | Clock Start Date: | 24 November 2016 |

Dr. Mark Sagarin was not present for discussion of this application.

The Committee noted the desire of Dr Sagarin to teleconference if possible (he was overseas).

When the allotted time came the Committee agreed to review the application on the basis of the new information supplied. The Committee agreed to Decline the application (for reasons stated below).

When Dr Sagarin teleconferenced much later, at an unexpected time, the Committee was already engaged with two researchers on two applications. The Chair informed Dr Sagarin of the decision, but because of time constraints was not able to discuss in detail, the reasons for declining, but said that these would disclosed in a letter.

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 was a resubmitted application (from a previously declined 15/NTB/215) with a modification to the project design a cover letter with detailed response (18 Nov 2016) by the researcher addressing issues raised in NTB’s decision letter of 2015.
2. This pilot study will be an observational convenience sample of patients presenting to New Plymouth and Hawera Hospital EDs. There will be no intervention. The only differences relative to standard care is (1) a timer will document the amount of time from the start of the relocation procedure until the time when the providers believe the shoulder is back in place and (2) the patient will complete a short (<1 minute) survey after the procedure. The relocation will be confirmed by x-ray.
3. The primary outcome measure is the time required to reduce the dislocation. Secondary outcome measures will be: (1) success versus failure, (2) use of various medications, and (3) patient satisfaction measures. Primary safety measures will include post-procedural fractures and nerve problems. All data will be entered into an anonymous database without any patient identifying information and analysed.

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 new Protocol supplied is inadequately brief in view of the fact that this will take place in an emergency department.
2. Specifically, the Protocol states the study is Observational. If this the case then the only primary study measure is the time measure. The Committee the researcher could not record medically related study data about a participant without their **prior** consent. If this data was collected as part of standard of care it would be a quality measure and would not be considered research.
3. On the question, of the satisfaction survey we question the usefulness of a question such as Q3 asking if they dislocated in the future, would they want the same procedure. How would they know? This questionnaire requires serious revision.
4. Further, when do you plan to administer this questionnaire? Immediately, on discharge, or when they are home. None of these issues are addressed in your Protocol.
5. Further to the Protocol. As this is occurring in an emergency department, you will require the cooperation of the emergency staff. The Protocol, as it stands, is not a sufficient briefing document for fellow clinicians and staff.
6. Further to the Protocol. We note that that there are different options for relocating shoulders. What are they? What is the problem at Tarnaki that justifies this research? Are there too many options, or are some of them outdated, are there better ways of doing it, are some procedures faster or better than others? None of this information is disclosed within the Protocol. Without a detailed Protocol we cannot make an informed decision on the merits or otherwise of this project
7. Further to the Protocol. Where is the search of the literature and references?
8. Hence our decision to decline due to lack of clinical justification for this study. The Committee could not see the benefit of a few seconds variation for shoulder dislocations and did not understand how timing the procedures would result in clinically meaningful information.
9. The Committee noted that if there is a clinical need to time the length of time taken to resolve a shoulder dislocation then the locality could initiate this quality measure itself without the need to seek HDEC approval. It does not require a research project to implement timing a procedure. Patients can provide feedback about their treatment as part of service evaluations.
10. Has the researcher discussed this project with hid Clinical Director and Senior Medical Officer? In our experience it is unusual to see a solo application from an ED environment, where the department functions on teamwork.
11. The Committee did not feel that 40 participants was a relevant sample size. Have you consulted a statistician on this matter/ what is the powering? None of this is discussed in the Protocol
12. In summary the Committee did not believe the study had scientific merit, or would generate benefit.
13. The Committee noted that the new application submitted by the applicant was not a health research study, and instead was a quality measure.
14. The Committee noted the letter to the HDEC requesting whether this data could be accessed as part of a quality improvement practice. The Committee noted that if this data was collected for clinical reasons then it could be used for audit and evaluation of services provided.
15. The Committee strongly suggested the researcher talk with the Locality research support office if the researcher was interested in running a larger study to generate clinically meaningful data. Research office support from a larger locality (e.g. the Awhina Knowledge & Research Centre at Waitemata DHB) might be available to the researcher if the locality cannot provider this support.
16. The Committee noted that there was not a research question to be answered within the application, and suggested further discussion with the locality research office could assist in using the research question to generate an appropriate study design.
17. The Committee noted that there was not a research question within the application, therefore there was nothing for the study to answer.

Decision

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

* Investigators should meet their obligations to communities by undertaking research that addresses important health problems. (Ethical Guidelines for Observation Studies para 5.1).
* Investigators should ensure any audit and related activities they undertake have the potential to improve health outcomes. (Ethical Guidelines for Observation Studies para 5.3).
* The Committee noted that there was not a research question within the application. Research can only occur when the design of the research can answer the study question. Scientific inadequacies in a study proposal have ethical implications. The scientific quality of a proposal should be such that the proposal’s objectives can reasonably be expected to be achieved. 5 (Ethical Guidelines for Observation Studies para 5.7).

## Review of approved studies

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| --- | --- | --- |
| **1** | **Ethics ref:** | **13/NTA/100** |
|  | Title: | Early Goal Directed Sedation vs. Standard Care Sedation |
|  | Principal Investigator: | Dr Colin McArthur |
|  | Sponsor: |
|  | Clock Start Date: | 27 June 2013 |

Dr Colin McArthur, Dr Paul Young and Dr Dick Dickson were present in person and by teleconference for discussion on this item.

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 reason for review

Approval for this study was reviewed on the basis of the following issues, which were raised by a formal complaint.

* The researchers did not approach the family of the participant to inform them of their family member’s enrolment into a clinical trial in an emergency context, even though there were numerous opportunities to do so (over the course of a number of days).
* The complaint was focused on the lack of resource and the procedures in place to consent and assent for this research study at the Wellington locality.

1. The Researcher(s) explaining the aims of the SPICE study
2. The Researcher(s) explained because sedation is required immediately, hence enrolment often occurs without consent and in many cases without the family’s views being taken into account.
3. The Researcher(s) explained that in 2013 the committee approved the protocol with regard to right 7(4) of the code of rights, and had discussed the best way to seek continued consent.
4. The Researcher(s) explained the process where after enrolment occurs urgently the family is approached when reasonable and practicable, to seek views of whether participant would want to continue participation (in the family’s views).
5. The Researchers acknowledged that the complainant and his mother’s experience was not in line with the approved protocol, and the researchers had not provided sufficient information in a timely manner.
6. The Researcher(s) explained the factors that led to this failure. These details were outlined in detail in two letters that were submitted to the Committee to consider, and were subsequently forwarded to the complainant.
7. The Researchers outlined the mitigation factors to stop this failure from occurring again, including the check lists, staffing practices and audit functions. HDEC also required increased reporting to ensure adequate monitoring of the trial.
8. The Co-ordinating Investigator confirmed best interests 7(4) was still being met by enrolment to this trial.
9. The Complainant reiterated that there were many cases that were note taken up to explain to the family that their family member was involved in a clinical trial.
10. The Co-ordinating Investigator explained the national level response to this complaint.
11. The complainant requested a letter sent to his mother about what has happened and what has occurred to remedy the situation.
12. The Complainant considered his complaint addressed sufficiently and accepted the HDECs ruling to approve the study, based on the improvements outlined by the researchers.

The Committee requested the following occur in order to ensure the study met ethical and legal standards:

1. Change the distinction for study drug arm and standard of care arm in terms of expected time to inform participants or their families.
2. Amend Participant Information Sheet wording to ensure the family members were not consenting on behalf of the participant, but rather they were providing their views on the wishes of the participant. Also amend the wording to ensure the clinician is enrolling through right 7(4).
3. Outline the site wide monitoring plans. Re-audit recruitment for the 2017 annual reports.

Dr McArthur said he would consult with steering committee regarding whether the protocol needed amending to specify a timeframe to gain retrospective consent. Currently timeframe for retrospective consent is not a data point hence is not monitored. Any issues with retrospective consent will not be brought to the attention of DSM.

Decision

The Committee decided that approval for this study should remain in place. This decision was made by consensus.

## 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:** | 15 December 2016, 12:00 PM |
| **Meeting venue:** | Ministry Of Heath - Via Teleconference |

1. **Problem with Last Minutes**

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

The meeting closed at 6.40pm