|  |  |
| --- | --- |
| **Committee:** | Northern B Health and Disability Ethics Committee |
| **Meeting date:** | 02 October 2018 |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Road East, Ellerslie, Auckland |

|  |  |
| --- | --- |
| **Time** | **Item of business** |
| 12:00pm | Welcome |
| 12:05pm | Confirmation of minutes of meeting of 04 September 2018 |
| 12:55pm | New applications (see over for details) |
| 12:55-1:20pm  1:20–1:45pm  1:45-2:10pm  2:10-2:35pm  2:35-3:00pm  3:00-3:25pm  3:25-3:50pm | i 18/NTB/157  ii 18/NTB/159  iii 18/NTB/160  iv 18/NTB/161  v 18/NTB/162  vi 18/NTB/163  vii 18/NTB/164 |
| 3:55pm | General business:  Noting section of agenda |
| 4:10pm | Meeting ends |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **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 | Present |
| Miss Tangihaere Macfarlane | Lay (consumer/community perspectives) | 20/05/2017 | 20/05/2020 | Apologies |
| 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 (intervention studies), Non-lay (observational studies) | 14/12/2015 | 14/12/2018 | Present |
| Mr John Hancock | Lay (the law) | 14/12/2015 | 14/12/2018 | Present |
| Mrs Jane Wylie | Non-lay (intervention studies) | 20/05/2017 | 20/05/2020 | Present |

## Welcome

The Chair opened the meeting at 12:30pm and welcomed Committee members, noting that apologies had been received from Miss Tangihaere MacFarlane.

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 04 September 2018 were confirmed.

## New applications

|  |  |  |  |
| --- | --- | --- | --- |
| **1** | **Ethics ref:** | **18/NTB/157** |  |
|  | Title: | Albinism - visual impact, ocular findings, and potential visual aids |  |
|  | Principal Investigator: | Dr Shuan H Dai |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 16 August 2018 |  |

Dr Samantha Simkin (PC) 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.

Background:

1. The proper term to use when referring to these children is “children with albinism”.
2. Albinism tends to be predominant in Pasifika people. Albinism is autosomal recessive so can be seen in smaller communities particularly the Pasifika community. Its recessive nature means it can skip generations but can end up in whole families if both parents have albinism.
3. Their place in society can depend on where in the world they are or on their family views on their condition. In some cultures they are revered and in others they may be persecuted. In NZ, there is not so much a stigma around Albinism but there are social issues particularly if they have a more severe form of the condition or if they stand out considerably from other members of their family.
4. Albinism varies from mild loss of pigment (ie, red hair & lighter eyes) to more severe loss (white skin, white hair and almost red eyes).
5. Melanin is a type of pigment and is needed in the eyes for normal development of visual function. It helps develop the Fovea which functions to provide fine central vision (used in reading and recognising faces). Lack of the pigment melanin means the Fovea is under developed which for children with albinism causes them to have poor sight. Pigments help block light going into the eye. Lacking pigment for those with Albinism makes it difficult for their eyes to block incoming light so everything tends to be glarer for them.

Summary of ethical issues (resolved)

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

1. The Committee asked if reading skills were more delayed because of Albinism.
2. The Researcher replied that children with Albinism often need more support.

Blind Low Vision Education Network (BLVEN) (which comes under the Ministry of Education) supports children with low vision and children who are blind in their learning while they are at school. It provides support services to ensure they are coping and enables these children access to curriculum in a way that suits them. In the majority of people with Albinism, their condition does not affect their cognitive ability or any other ability so they have every possibility to succeed as any other child. Their main barriers to learning are that they have reduced vision and they struggle in bright light.

The Committee noted that the study involves two parts, Observational (part A) and Intervention (part B).

Observational part (Part A):

1. The Committee questioned why the observational part of this research is being done without consent.

The Researcher stated that BLVEN runs a clinic (covering Optometry, Opthomolgy and Paediatrics) in Auckland for those enrolled with them and they can fly these children to Auckland to access their clinic. Not all the children enrolled will go through the clinic and if children do not attend, medical professionals send their referrals to the clinic for its assessment to determine appropriate requirements to assist the children in their schooling, based on the funding they receive. The clinic operates as a medical clinic in an educational setting.

1. The Committee questioned if those using the clinic’s services are aware that their records would not only be used to manage Albinism but could also be used in research.

The Researcher’s understanding is that they can access the data in a de-identified form from BLVEN. The research team will send out a request to families seeking their consent to access their child’s records from BLVEN for the purpose of research.

1. The Researcher confirmed that all those whose data they would access would also be the people they would send the questionnaire to.
2. The Researcher confirmed that getting in touch with families would be done by mail and this mail out would be done on their behalf by BLVEN.
3. The Committee questioned if it would matter if a number of people did not agree to the accessing of their records or is the accessing of records only for the purpose of informing part B of the study.
4. The Researcher replied that there is not any good data nor any publications on Albinism in New Zealand. BLVEN will be a good source for this but it is also limited as it only covers a certain group - children whose vision is worse in the ages of 6 to 18 so not everyone with Albinism will be captured. The data they get will not be generalizable but will be more of a snap shot of Albinism in New Zealand. The data gained would inform of the potential benefits of the contact lens fitting.
5. The Committee stated that the filling in of the Questionnaire by families and its return to the research team would be acceptable as an indication of consent by families. However, it must be made clear to families that this is the case.
6. The Researcher confirmed that potentially those recruited to part A would also go onto part B.
7. The Committee questioned what the lower age of recruitment would be, would it be 5 year olds or 7?

The Researcher stated for general information purposes they would collect from a wider group so the lower range of recruiting would start at 5 year olds. However, to ensure that contact lens are being worn reliably and safely they would move this lower range of recruiting to 7 year olds.

The Committee advised that it should be made clear to families that 5 and 6 year olds will included in the recruitment for part A of the study but only 7 years olds and above would be eligible to take part in part B.

Interventional part (part B):

1. The research team plan to recruit up to 60 participants with some room for attrition

In terms of accessibility they run a national programme but the clinic is based in Auckland which will limit the number of people that can be recruited.

1. The Researcher confirmed that the questionnaire is for parents and stated that they did not expect 18 year olds or older to be part of the study as those in the BLVEN programme tend to leave at 18.
2. The Committee asked if children’s vision will be sufficient enough to read the information sheets.
3. The Researcher informed that they plan on using a large sized print on the information sheet to assist with this. They will also read the form to the children and help them fill it out.
4. The Committee recommended that details of the information sheet could also be recorded onto a video/audio and uploaded to a site where participants could access it via their IPads.
5. The Committee asked after the cost of the lens, especially once the study is completed.

The Researcher replied that the lens were specially made so would be not available off the shelves. The lens’ suppliers had advised that they could be made available after the study through participants’ optometrists. For eye health reasons, lens need to be prescribed by an optometrist and wearers are expected to have regular check-ups.

1. The Committee requested participants are made aware up front what they can expect when choosing to use the lens.
2. The Researcher explained that the contact lens with a tint can last for a year. These can be available at a cost of $80 a pair. The Researcher confirmed that they will talk to suppliers about continuing to make this price available to participants once the study has finished. The Researcher will ask the suppliers to put this in writing. The Researcher added that on top of this cost there will be monthly costs of $20 for cleaning solution.
3. The Committee were concerned about the on-going costs associated with lens and asked if families could access some sort of financial assistance.
4. The Researcher responded that government could fund those that can prove that lens improves their vision more than spectacles. This may help some families. Funds to assist could be accessed from Albinism Trust and BLVEN but no formal procedure has been set up for this so could not promise.

Both the Researcher and the Committee agreed that this may be easier to guarantee once the study is completed and the results are known.

1. The Researcher stated they can get sample packs of cleaning solutions for families but could not do this indefinitely. They will be happy to support them in transition while looking for other funding options.
2. The Committee requested it be made clear to participants that they would not be given access to lens at the end of the study but, as they may benefit from them during the study this could allow for funding to be accessed for continuing lens use upon study completion.
3. The Committee asked about using Community Services Cards to fund lens following study completion.
4. The Researcher advised that with Community services cards, those under the age of 15 receive an amount of $287.50/year for eye exams or optical appliances. This amount could be used to purchase lens but a special request would need to be made to obtain the cleaning solution so this may not be guaranteed.

The Researcher emphasised that this amount is fixed so if a participant may need additional spectacles or tinted lens it could take their payment to beyond the amount provided by the Community Services Card. The Researcher stressed that this option would only be available for those 15 years and younger.

1. The Committee viewed this information as important and thereby should be disclosed to participants. Let participants know of entitlements they can access to allow them to continue with lens use once the study is completed. This can include referrals.
2. The Researcher confirmed that the company is not going to be receiving any data.

Application:

1. The Researcher confirmed that BLVEN would be responsible for governance of the study.
2. The Committee decided as this is the case then BLVEN would be recognised as the sponsor.
3. The Committee noted in question 2.4 of the application that it states data will be stored partially de-identified and asked why.
4. The Researcher explained while seeing participants over multiple follow-ups, data will be partially de-identified so they can be tracked but once the study is completed, participant data will kept in an anonymised form (no identifying markers linked to them and not able to be re-identified). The research team will also provide participants with the exact constructs of their lens to share with their optometrists for fitting purposes. This should help reduce optometrist costs for participants.
5. The Researcher stated that advertising would not be used as they are not involving anyone outside of the existing database.
6. The Researcher confirmed that they would not be using kaupapa Maori research methodology and acknowledged that question p.4.4 was answered incorrectly.
7. The Researcher stated Maori consultation had been made with Ngati Kapo Maori who represent Maori who are visually impaired. The Ngati Kapo Maori group will be noted as Maori contact on the PIS.
8. The Committee questioned if interpreters would be provided for Pasifika participants.

The Researcher replied that due to lack of funding it would not be likely and asked the Committee for suggestions on how to address this.

1. The Committee suggested that participants be encouraged to bring along family members/friends to help with interpreting.
2. The Researcher stated that it would be difficult to find interpreters for the specific Pasifika groups (Niuean & Tokelauans) affected by Albinism due to their small numbers in the community.

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 suggested the research team seek at the same time, participant consent to look at their BLVEN data and to request they fill out a questionnaire. These families should be allowed the option to choose the level to which they want to be involved (eg, fill out the questionnaire but not consent to their BLVEN data being accessed).
2. Please provide a copy of the introductory letter being sent out to families. It should state the researchers would like access to their child’s records.
3. Please ensure families are aware that completion of the Questionnaire and its return will be indication of consent.
4. Please be clear to participants that not everyone that is involved in part A of the study may have the opportunity to be involved in part B and explain the limitations.
5. Please note that the age of consent in New Zealand is 16 and not 18 so young adults aged 16 and above can have their own consent as opposed to parent/guardian consenting on their behalf.
6. The Committee advised it should be made clear to families that 5 and 6 year olds may be recruited for part A of the study but only 7 years olds and above would be eligible to take part in part B.
7. Questionnaire for the progress 1 and 2 visits has 2 questions that asks for a comparison of the lens types. However, at progress 1 visit there will be no lens to compare. Please re-think this, perhaps make two separate questionnaires

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

1. Please be clear to families that their child’s records will be accessed for the purpose of this research.
2. Please ensure the following participant information sheets are prepared;
3. Participant Information Sheet (PIS) for ages 16+ and consent given on their own behalf. Youth aged 16 and over may talk to parent/guardian about the study but decision should be their own.
4. Please avoid using technical terms such as impact.
5. Parent/Guardian PIS for parents/guardians to consent on behalf of children younger than 16. Your existing PIS is appropriate for this but you need to use the term “your child” (eg,” is your child wearing spectacles”).
6. Assent forms for children. 7-11 and 12-15 – only for intervention part of the study. See <https://ethics.health.govt.nz/guides-templates-forms-0>, Forms and templates section for information on and examples of assent forms.
7. For visually impaired children, please discuss the information with them and record their verbal assent.
8. Please inform participant GPs, Ophthalmologists and Optometrists of participant’s involvement in the study and ensure they are notified of any abnormal findings should it arise.
9. Under the section, “What does my participation involve?” it is not obvious what you intend to do. The Committee’s understanding is that one lens type is used for 4-six weeks then there is a cross over to the second lens type for 4-6 weeks after which, participants choose their preferred type for next 3 months. Please make this process clear.
10. Please include the Maori support contact details.
11. Please ensure participants are aware of the funding option provided by the Community Services card and all the details associated with this. Let participants know of entitlements they can access to allow them to continue with lens use once the study is completed. This can include referrals.

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)
* Please be clear to participants that not everyone that is involved in part A of the study may have the opportunity to be involved in part B and explain the limitations (Ethical Guidelines for Intervention Studies, paras 6.6 and 6.7)
* Please ensure families are aware that completion of the Questionnaire and its return will be indication of consent (Ethical Guidelines for Observational Studies,para 6.28)

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

|  |  |  |  |
| --- | --- | --- | --- |
| **2.** | **Ethics ref:** | **18/NTB/159** |  |
|  | Title: | DYNAMIC-III |  |
|  | Principal Investigator: | Dr Mark Jeffery |  |
|  | Sponsor: | The Walter and Eliza Hall Institute (for the Australasian Gastrointestinal Trials Group) |  |
|  | Clock Start Date: | 13 September 2018 |  |

Dr Mark Jeffery (CI) 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. There is frustration amongst Oncologists around the high number of overtreatments of patients with chemotherapy and that treatment is not always successful in treating recurrence.
2. Generally it may only directly benefit 10-15% of patients that receive adjuvant chemotherapy after bowel surgery.
3. Oncologists are always looking for prognostic markers that might better define those patients that need treatment and those that benefit from it.
4. Several studies have uncovered an exciting new find in “circulating tumour DNA” genetic testing. If this test can detect this DNA several weeks after surgery then it is highly suggestive that micro metastatic disease is present and those patients are at greater risk.
5. However, if this result is negative then these patients are unlikely to develop further problems and they could be spared side effects of chemotherapy. This is potentially exciting as it may lead to personalised approach to each patient as to whether they need treatment. This study design hopes to test this hypothesis.
6. With genetic testing taking place, there’s a possibility that it will pick up patients that develop bowel cancer because they are born with inherited susceptibility which will have implications for other family members. The Researcher views this as good thing rather than as an ethical problem.

Summary of ethical issues (resolved):

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

1. The Researcher confirmed that both the standard of care arm and the intervention arm will receive blood tests.
2. The Committee questioned that if the research team was confident about the blood tests then ethically the standard of care arm should also be told of any findings.
3. The Researcher replied the test is new and potentially it might drive a new strategy but it is untested so has to be blinded at this stage to prove the hypothesis. Additionally if findings were revealed to everyone the study’s design will be undermined.
4. The Researcher confirmed that he believes that the sensitivity in stage 2 colon cancer will be similar to that in stage 3.
5. The Committee advised that it usually sees studies apply medication as the intervention and the biomarker as the future unspecified research (FUR) component, which has its own separate Participant Information Sheet (PIS). However, this study is the opposite. Essentially in this study, it is the biomarker testing which is applied first which then determines the therapeutic intervention.
6. The Committee noted the addition of another medication; a third chemo drug (Irinotecan) and asked to what extent is it a major aspect of the study. Is the study a test or a test and a drug combination?
7. The Researcher advised that the addition of the drug is more of a strategy. A strategy that sees de-escalation for a negative test result and an escalation for a positive test result.

Implications of positive test result is that the patient will do badly therefore the response is to propose escalation of the drug (this regimen is not standard of care). This regimen is used in metastatic disease and a similar regimen is used in adjuvant pancreas cancer. There is evidence that it does improve survival after patients have had pancreas cancer. This is an appropriate response to positive circulating DNA result but cannot point to any evidence of its use in the adjuvant setting for colon cancer. There is still some speculation as to whether it is the right thing to do.

1. The Committee questioned why there seems to be an argument in the PIS (and throughout the application) about the genetic testing not necessarily being biomarking.
2. The Researcher agreed and will read over the PIS more thoroughly and make the appropriate adjustment.
3. The Committee wanted to know what would happen to participants on less medication after surgery should the hypothesis about genetic testing be incorrect (ie, not a way to optimise post-surgical chemotherapy). Is there potential for harm for these participants?
4. The Researcher replied that the only potential harm he foresees is that patients will have recurrence.
5. The Committee noted that chemotherapy being applied is less than that in standard of care and wanted to know if a safety protocol is in place to identify if things start to go wrong in the study.

The Researcher replied that they would look at the rates of de-escalation.

1. The Committee were aware that the study is Australian led but asked if the research team could include ethnicity details.

The Researcher said he would make the request to the Australian lead site but could not make any promises.

Summary of ethical issues (outstanding):

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

1. The Committee requested the PIS clearly states that the study involves two parts:

a) genetic test that may determine drug intervention post-surgery and

b) addition of new drug that is not standardly used and has not been tested in

stage 2 bowel cancer.

1. The Committee asked that it be made clear that the term “archival samples” refers to tissue recently removed in surgery (ie, 5 or 6 weeks old).
2. The Committee noted the study will keeping participant information in an identifiable form and asked if in this form it will be sent overseas (page 9).

The Researcher replied that this statement is only relevant for the Australian sites.

Please ensure this section of the PIS is tidied up to report correct information.

1. Please amend the PIS for repetition as there seems to be a lot of this (eg,number
2. Please review and make sure it is simplified.
3. Please stick to common names for medication to make it easier for participants.
4. There are a lot of Australian references throughout, please remove these or remove and use New Zealand references where required.
5. The Committee were concerned about the potential for confusion by participants on whether all would receive the results of genetic testing. Please make sure it is clear in the PIS exactly the type of results each group can expect to receive. (eg, familial condition versus tumour related).

Future Unspecified Research

1. The Committee requested it be made clear to participants that the future unspecified research (FUR) segment of the study will not be subject to New Zealand laws once it is overseas. To ensure people are aware that FUR is optional, please create its own separate PIS/CF document.

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 Mr John Hancock and Mrs Leesa Russell.

|  |  |  |  |
| --- | --- | --- | --- |
| **3.** | **Ethics ref:** | **18/NTB/160** |  |
|  | Title: | ZEST 2 |  |
|  | Principal Investigator: | Professor Peter Gilling |  |
|  | Sponsor: | Zenflow Australia Pty Ltd |  |
|  | Clock Start Date: | 20 September 2018 |  |

Ms Rachael Hamill (Research team) & Deborah Bell (Sponsor) was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of ethical issues (resolved):

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

1. The Committee noted that the device involves is a little spring that holds the urethra open and should help with urinary problems with middle aged men and above.
2. The Committee questioned what happens when the spring is removed.
3. The Researcher(s) stated that based on the safety & feasibility study already completed in New Zealand (n=13 participants) participants had their devices removed at various time points, longest time before finally being removed was 20 months. These participants did not suffer any detrimental issues (ie, the device did not break apart nor did it move around in the pelvis).
4. The Committee noted the study has two stages and will conduct a roll in period so surgeons can get use to the technique involved. How many patients will be involved in NZ?
5. The Researcher(s) explained that they plan to have 10 patients in total. Initially this study was meant to be conducted in Mexico then it was decided to add the two NZ sites already involved in the safety & feasibility study to allow for continuity and enable these sites to also take part in the subsequent study aimed at getting C mark regulatory approval in Europe. Although the delivery system has been slightly modified between this study and the feasibility study, the procedure between the two, is essentially very similar.
6. The Researcher(s) confirmed the roll in period will not be conducted in New Zealand.
7. The Researcher(s) confirmed an analysis will be done after the first participant and if successful then will continue enrolling. Another assessment will be done at the 6 week point.
8. The Researcher(s) explained the Data Safety Monitoring Board will review the first 10 participants. Five have already been treated in Mexico and it is hoped that the next five will be treated in New Zealand.
9. The Researcher(s) confirmed the two sites in this study were also involved in the safety and feasibility study, one in Tauranga and the other in Nelson. The surgeons at these sites are already familiar with the device.
10. The Committee queried the risks involved in keeping the device implanted for those that choose to at the end of the assessment (ie, after 2 years).
11. The Researcher(s) replied that as far as they are aware there are none. The stent uses long term titanium and nickel material. If patients choose to keep the device in long term, they will be monitored as per standard of care by their urologist on an annual basis. If it needs to be completely removed because of recurrent infection there is a retrieval tool at the site that can be used to pull it out. However, it is anticipated that any patients with recurrent infection will go on to an alternative surgical intervention.
12. The Committee focused on the potential risks list particularly risk number nine which stated that 35 out of 100 could expect to get urinary obstruction. How does this compare with other stents?
13. The Researcher(s) replied this proportion was based on the safety & feasibility study data, other stents and the Uralis device. It would be slightly lower than other stents which have now been discontinued as they caused issues long term and contained more metal. The more metal there is in a stent, the greater the risk of ingrown tissue.
14. The Committee asked if participants would be candidates for a TURP operation.
15. The Researcher(s) replied that if participants have had a TURP operation then they would not be a candidate for this procedure as they would not have any remaining mass prosthetic tissue. All other participants however, could potentially be candidates for TURP although the more likely are those who have mild to moderate disease process, had drug therapy that failed and are unwilling to continue with it. There are prosthetic urethra lens limitations and prosthetic volume limitations for this device, so large obstructive prostrate will need to undergo a de-bulking procedure.
16. The Committee questioned what treatment participants would receive if this study was not being conducted.
17. The Researcher(s) responded the participants would be on waiting lists for TURP or a homing neucleation for prostrate.
18. The Committee asked how entry into the study will affect waiting times for participants. Will they have an advantage by being offered the study and if there is, will they be told of it?
19. The Researcher(s) stated that if participants are on the waiting list, chances are they will have treatment sooner but, they are on the waiting list for a surgical procedure rather than this device and this device holds that surgery off for maybe a few years. The Researcher(s) added that participants recruited were from the waiting lists, GP patients and patients of their private practice (Tauranga Urology).
20. The Committee were a little baffled by this statement as their understanding of the application is the study was only targeting people who had been referred for TURP
21. .The Researcher(s) confirmed that Maori kaupapa methodology was not being used in this study so question p.4.4 of the application had been answered incorrectly.
22. The Committee stated that claims should not be made to suggest that taking part in the study will expedite treatment. The same goes with claiming benefit from involvement. It may be beneficial but risks are being taken so the treatment may turn out to be less advantageous.

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 participants are only being given one option for when to opt to have the device out with assistance from the study team that is, at 2 months after the study ends (page 5, Participant Information Sheet.
2. The Committee asked what would happen should participants want the device removed after 3 months.

The Researcher(s) replied participants will only get assistance from the study team (including costs) to remove the device if they choose to at 2 months after the study. The sponsor can only be responsible for participants over a finite time. If participants want the device removed outside the 2 month period then they are no longer part of the study and they will have to discuss various treatment options with their urologists.

1. The Committee stressed that this is unacceptable and reminded the Researcher(s) that the study team and sponsor are obliged to take care of participants while the device is still implanted. There must be care for participants and an arbitrary timeline should not be put on it.

The Committee do not expect participants to incur costs from participation in a clinical trial. If there is a late effect or long term serious adverse event from the device, it is the responsibility of sponsor and the study team. The sponsor must incur the costs of the study device removal at any time point done primarily under care of the principal investigator and study team or alternative arrangements will be made.

The Committee strongly emphasised that responsibility remains with the sponsor and the study team.

1. The Committee acknowledged the peer review from Chris Crampton, Biostatistician and requested an independent peer review from someone with a clinical background and experience in urology devices. This should allow for an overview of safety and clinical indications.

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

1. Please state where data will be kept, how it will be kept and in what form (eg, electronic data capture system in de-identified form at the Tauranga Urology Research Facility)
2. Please be clear that no tissue will be sent overseas and testing will be done locally.
3. Please correct the following statement; “No tissue specimen will be required as part of this study”. This is not accurate as HDEC’s classifies blood as tissue.
4. Please include a landline/mobile number for contact Peter Mason to make it easier for participants to reach him should they have specific concerns.
5. Please check that it is clear in the PIS that participants who do not continue onto stage 2 will continue to be followed up to the 2 year point.
6. Please list what alternatives would be for participants if they do not make it into the study.
7. In the Consent form please ensure only the truly optional statements have yes/no tick boxes next to them (ie, if a participant ticks no, they can still take part in the study). Please remove clause 9 as it is not appropriate for this study.
8. Please include the following HDEC required compensation statement (latest version):

As this research study is for the principal benefit of its commercial sponsor [insert name], if you are injured as a result of taking part in this study you **won’t** be eligible for compensation from ACC.

However, [insert name] has satisfied the [ insert name] Health and Disability Ethics Committee that approved this study that it has up-to-date insurance for providing participants with compensation if they are injured as a result of taking part in this study.

New Zealand ethical guidelines for intervention studies require compensation for injury to be at least ACC equivalent. Compensation should be appropriate to the nature, severity and persistence of your injury and should be no less than would be awarded for similar injuries by New Zealand’s ACC scheme.

Some sponsors voluntarily commit to providing compensation in accordance with guidelines that they have agreed between themselves, called the Medicines New Zealand Guidelines (Industry Guidelines).These are often referred to for information on compensation for commercial clinical trials. There are some important points to know about the Industry Guidelines:

* On their own they are not legally enforceable, and may not provide ACC equivalent compensation.
* There are limitations on when compensation is available, for example compensation may be available for more serious, enduring injuries, and not for temporary pain or discomfort or less serious or curable complaints.
* Unlike ACC, the guidelines do not provide compensation on a no-fault basis:
* The Sponsor may not accept the compensation claim if:
* Your injury was caused by the investigators, or;
* There was a deviation from the proposed research plan, or;
* Your injury was caused solely by you.
* The injury was caused by <<NAME OF COMPARATOR DRUG>> (include only if holds true for specific study)

An initial decision whether to compensate you would be made the by the sponsor and/or its insurers.

If they decide not to compensate you, you may be able to take action through the Courts for compensation, but it could be expensive and lengthy, and you might require legal representation. You would need to be able to show that your injury was caused by participation in the trial.

You are strongly advised to read the Industry Guidelines and ask questions if you are unsure about what they mean for you.

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, taking into account the suggestions made by the Committee (Ethical Guidelines for Intervention Studies, para 6.22)
* Please provide evidence of favourable peer review of the study protocol (Ethical Guidelines for Intervention Studies, Appendix 1. HDEC peer review template can be found at <https://ethics.health.govt.nz/> under the Quick Links section).
* Participation in a study should not entail unfair burden on participants (Ethical Guidelines for Intervention Studies, para 4.5)

This following information will be reviewed, and a final decision made on the application, by Mrs Maliaga Erick and Mrs Jane Wylie

|  |  |  |
| --- | --- | --- |
| **4.** | **Ethics ref:** | **18/NTB/163** |
|  | Title: | SUBCUTANEOUS TIBIAL NERVE STIMULATION FOR URGENCY URINARY INCONTINENCE: A FOLLOW-ON STUDY |
|  | Principal Investigator: | Dr. Sharon English |
|  | Sponsor: | Valencia Technologies Corp. |
|  | Clock Start Date: | 20 September 2018 |

Stacey Chamblis and Ted Salin (Valencia Technologies Corp) were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study:

1. This is a follow up study for the safety and effectiveness trial of eCoin tibial nerve stimulation in 30 subjects with refractory overactive bladder as defined by the American Urological Association.

Summary of ethical issues (resolved):

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

.

1. The Committee noted the annual report relating to the safety and effectiveness part of this study (HDEC reference-17/NTB/31) which was submitted in April, states that 19 participants had been recruited in New Zealand.
2. The Researcher(s) confirmed this and the fact those recruited there would have the

opportunity to also take part in this follow up study.

1. The Committee questioned how risks of the misplacement of device were being handled now that the research team have experience with the device
2. The Researcher(s) acknowledged that during the first implant in New Zealand (in the safety and effectiveness trial of the device), one investigator had misused the measurement tool which led to a slight but still meaningful misplacement of the device. As a result measurements were not being taken at the correct places on the ankle.

The research team worked to correct this by seeking assistance from Surgical Consultants, revising the implant manuals and looking over pictures of every implant done thereafter. As a result they were able to spare 46 implants from this issue.

1. The Committee asked for an explanation of the 10 point improvement in quality of life score in the feasibility study. What does it mean to participants?
2. The Researcher(s) replied that in the survey the 10 point improvement is considered clinically significant and added that a survey that would be more meaningful to participants is the “Patient Global Impression of Improvement Survey”. This gauges how much better patients feel following therapy (choice of; “better”, “much better “and “completely better”). The Researcher(s) did not know the exact scoring so would have to work it out and stated that the other indicator would be if 70% of patients are getting at least 50% or better in their urinary incontinent symptom which is very successful in an overactive bladder.
3. The Committee stated it would be telling how many of 19 choose to re-implant and this would be a good indication of how many felt good about the device.

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 that the insurance certificate be renewed as it has expired. It also needs to be study protocol specific and include New Zealand as a territory.
2. The independent peer review needs to be updated for the current protocol. The person that reviewed the earlier phase of this trial could review this phase or an independent peer review can be sought from an urologist.
3. The Committee strongly emphasised that the study cannot be stopped simply for reasons of commercial interest or public relations which is indicated in question r.1.6 of the application
4. The Committee requested a copy of the Indemnity certificate for Co-ordinating Investigator – Sharon English.
5. The Committee asked the research team to look into the conditions of the Maori consultation for the earlier phase of study. If it states that further consultation should be made on any following phases then please ensure Maori consultation is attended to.
6. The Committee questioned if medical conditions (ie,skin healing due to device implant and explant) could be part of exclusions or is it based on the surgeon’s assessment at the time.
7. The Researcher(s) replied that as they are not sure, they would refer this to either their peer reviewer or their surgical consultant.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (Participant Information Sheet/Consent Form (PIS/CF) :

1. Please make it clear that the battery life is only good for 3 years and outline the implications for participants that choose not to have the device removed.
2. The HDEC reference number needs to be updated.
3. Please thoroughly review for technical language and use lay language where ever possible.
4. Please include a picture/diagram of where the device will be placed on the leg. This may help with footwear choice to avoid rubbing.
5. Please bold the statement on MRI.
6. The Committee questioned if all 19 participants (from the initial phase of the study) have had their devices taken out.

The Researcher(s) replied that only 2 have.

The Committee questioned why this was the case. Will the device be re-activated or will another be added?

1. The Researcher(s) explained that the device will be replaced but: (i) they want the ability to study the re-implantation of a device that has a battery life and part of the therapy is that it will be replaced when the battery dies.
2. (ii) because they made changes during the study to the re-programming of the device, some batteries will be depleted sooner which was not part of the original projection. This offers the opportunity for a new, next generation device which has a longer battery life and its programming option is more advanced so it will not have to be re-set (causes reduction in battery life). This will allow participants the opportunity to continue to receive therapy.
3. The Committee noted the PIS fails to say this.

As the Committee understands the information; 19 participants who could have had the device left in must have had it explanted. It was hard to understand why they would do that and why they would then want it re-implanted. The fact though, is participants have not had the device explanted but will, and another will replace it. This needs to be clear in the PIS and include information about the extension to the battery life.

1. The Committee questioned what would be done should some participants not want to be part of the study and have the new device implanted. Would the original devices be removed given the battery lives are expiring or expired?

The Researcher(s) responded that it will be removed. There is a range so not all the batteries will be expiring. The participants will be given the options to either have their devices explanted or get a new device. All options need to be explained clearly to participants including that they can have the device taken out without a new one going in.

1. Please remove the statement on the voiding diary at baseline, page 3.
2. Please include HDEC’s most current commercial sponsor compensation statement which is worded as follows ( also found in HDEC’s PIS/CF template at <https://ethics.health.govt.nz/> ):

As this research study is for the principal benefit of its commercial sponsor [insert name], if you are injured as a result of taking part in this study you **won’t** be eligible for compensation from ACC.

However, [insert name] has satisfied the [ insert name] Health and Disability Ethics Committee that approved this study that it has up-to-date insurance for providing participants with compensation if they are injured as a result of taking part in this study.

New Zealand ethical guidelines for intervention studies require compensation for injury to be at least ACC equivalent. Compensation should be appropriate to the nature, severity and persistence of your injury and should be no less than would be awarded for similar injuries by New Zealand’s ACC scheme.

Some sponsors voluntarily commit to providing compensation in accordance with guidelines that they have agreed between themselves, called the Medicines New Zealand Guidelines (Industry Guidelines).These are often referred to for information on compensation for commercial clinical trials. There are some important points to know about the Industry Guidelines:

* On their own they are not legally enforceable, and may not provide ACC equivalent compensation.
* There are limitations on when compensation is available, for example compensation may be available for more serious, enduring injuries, and not for temporary pain or discomfort or less serious or curable complaints.
* Unlike ACC, the guidelines do not provide compensation on a no-fault basis:
* The Sponsor may not accept the compensation claim if:
* Your injury was caused by the investigators, or;
* There was a deviation from the proposed research plan, or;
* Your injury was caused solely by you.
* The injury was caused by <<NAME OF COMPARATOR DRUG>> (include only if holds true for specific study)

An initial decision whether to compensate you would be made the by the sponsor and/or its insurers.

If they decide not to compensate you, you may be able to take action through the Courts for compensation, but it could be expensive and lengthy, and you might require legal representation. You would need to be able to show that your injury was caused by participation in the trial.

You are strongly advised to read the Industry Guidelines and ask questions if you are unsure about what they mean for you.

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. The Committee questioned how long the device will remain in the body.

The Researcher(s) replied that the battery will last 2-3 years and the sponsor will pay for its explant but only if it occurs within the 3 years.

Please state this in the PIS and be clear that the device will be explanted and cannot remain in the body with an expired battery.

Decision

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

* Please provide evidence of favourable peer review of the study protocol (Ethical Guidelines for Intervention Studies, Appendix 1. HDEC peer review template can be found at <https://ethics.health.govt.nz/> under the Quick Links section).
* 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)
* Studies should not be terminated simply for reasons of commercial interest or public relations (Ethical Guidelines for Intervention Studies, para 6.65).
* Please submit evidence of Co-ordinating Investigator indemnity (Ethical Guidelines for Intervention Studies, para 4.20)
* Please submit evidence of current sponsor insurance. It should be study protocol specific and include New Zealand as a territory (Ethical Guidelines for Intervention Study, para 8.4).
* Please ensure any potential cultural and ethical issues relating to Maori are addressed through appropriate engagement with Maori (Ethical Guidelines for Intervention Studies, para 4.7 – 4.10)

The Committee invites you to re-submit your application to this committee and looks forward to reviewing it.

|  |  |  |  |
| --- | --- | --- | --- |
| **5.** | **Ethics ref:** | **18/NTB/162** |  |
|  | Title: | Postnatal depression in mothers of babies born by Caesarean section |  |
|  | Principal Investigator: | Dr Richard Carpenter |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 20 September 2018 |  |

Dr Richard Carpenter (CI) and Dr Alyssa Page (Co-Author and Senior House Officer) 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 study is an intervention of mothers at risk of post natal depression. The aim is to recognise Post Natal Depression (PND), raise it with mothers, help reduce its rates and increase rates of mother’s seeking help for PND.
2. The study is part of RANZCOG training and will be published.
3. The research team approximated that there could be up to 50% of mothers in the North Shore that may suffer from PND. Currently very little is being provided on preventing or treating PND. Many mothers suffer in silence and are un-supported, only when it gets serious is it recognised to treat. Ideally intervening immediately is what the research team want to focus on.
4. Standard of care is inconsistent.
5. Compared to other causes maternal mortality (such as, haemorrhage, pre-eclampsia) receive a lot of attention but PND is the number one killer of mother’s in New Zealand far and above, through suicide.
6. PND is common. The RANZCOG, International Colleges, European Colleges and British Colleges all recommend screening early in the pregnancy (ie, as soon as pregnancy is known).

Summary of ethical issues (resolved):

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

1. The Committee questioned if there are predictors of PND.

The Researcher(s) replied that there are risk factors. Some studies done have shown that they only protect 20% of people who go on to develop PND. The research team’s argument is that the risk stratified approach is not effective as it can miss up to 80% of people who develop PND without strong risk factors

1. The research team plan to use intervention opportunities that exist.
2. The Researcher(s) explained that women who have a caesarean section are reviewed the next day by a Junior Doctor/House Officer. The junior doctors talk them through common parts of post-partum care (wound care or breastfeeding) but do not talk about mental health issues.
3. At this point a less than one minute talk on PND in context of all the other information, will be made stating that PND is real, can cause problems and if they need help to get it early as there are effective treatments. The women will then be give an information pack to allow for self-screening for PND, immediately and then at 6 weeks later.
4. Results will be linked to local support structures in an algorithm that the women can follow.
5. The women will be followed up with a text reminder.
6. The Researcher(s) explained that before work each morning/ before the morning hand over either Dr Richard Carpenter or Dr Alyssa Page will recruit all women that had a caesarean section the previous day. The idea is to conceal that the study focuses on PND specifically.
7. The Researcher(s) will tell the women that they are looking at the aspects of care for women who have delivered by Caesarean-section. They will state in general what it involves in terms of reading &intervention, receiving text and follow up 8 weeks later when validation happens.
8. The Researcher(s) reported that if a women enquires specifically on what the study is about then she would be told upfront that it is a study on PND. This fact will be noted and this information will not be included in the analysis in order to avoid the Hawthorne effect and therefore its implications on the study.
9. The Researcher(s) have talked with several senior colleagues and cannot see anyway to evaluate whether an intervention that raises awareness about PND is actually successful if the consenting process raises awareness of PND.
10. The Committee raised the point that where there is concealment, it needs to be balanced by a de-brief. When and how will this happen?
11. The Researcher(s) stated at 8 weeks post intervention:
12. the women will be contacted,
13. the research team will explain that they has been part of a study on PND,
14. the intervention group in relation to the control group will be explained,
15. the women will be asked complete a perform scale questionnaire to assess her risk for PND at that stage
16. the research team will link her with standard resources.

By following up at 8 weeks, the research team are acting in line with the College guidelines and still within the best bundle of standard of care.

1. The Researcher(s) hoped that the Committee would give them a bit of leeway on the consent process so the study could avoid confounding.
2. The Committee were worried that the women could feel as they were tricked (thus lose trust) if they were not made fully aware of being part of the PND study until after the fact. The Committee recommended that study state that it will be looking at “aspects of mental health”
3. The Committee confirmed that the general public would not necessarily associate mental health with postnatal depression. For most people, “Mental health” would not be specific and it would be associated with issues such as anxiety, baby blues or loneliness.
4. The Committee wanted to know who would do the recruiting and take consents.
5. The Researcher(s) replied that Dr Alyssa Page, charge midwife-Eleanor McQueen and Dr Richard Carpenter would be the only 3 doing recruitment and, they will not be involved in the intervention.
6. The Researcher(s) stated that throughout the study it will be whichever House Officer (HO) is available on the day that carries out the intervention.
7. The Committee asked how the research team will make sure, considering all the demands on the HOs, that the quality of the delivery of the information and the consent is at the level that the team expects.
8. The Researcher(s) explained that the HOs only hand out the pamphlet and say very little. They will not be taking consent. Only Dr Page, Ms McQueen and Dr Carpenter will take consent.
9. The Committee asked if the HOs would be educated on their approach to women and if they would use a standard script.
10. The Researcher(s) replied that they would talk the HOs through their roles at morning meetings and make sure the approach used is standardised.
11. The Committee asked what would be done should an HO decline to help with the study or is too busy.
12. The Researcher(s) replied that they would not pressure the HOs to take part and would just ask other HOs.:
13. The Committee raised the issue of informed consent and advised that a basic component of informed consent is it should be informed by an adequate understanding of any information that is relevant to the decision making where ”adequate understanding” needs to be information relevant for the purpose which they are enrolled in study/ sufficiently connected to the purpose of the study.

To what extent has this been discussed with the peer reviewer and what advise was given?

1. The Researcher(s) responded they had planned initially to apply fully informed consent for participant information sheet shown in appendix A, version 1. They then talked to Wayne Miles, Psychiatrist at North Shore Research Centre and he suggested that concealment be used in the study. The peer review does say that fully informed consent will jeopardise the validity of the study.
2. The Researcher(s) confirmed that participants are not exposed to increased risk of harm.
3. The Committee reflected on the study’s population focus. This should consider the population which is most at risk of PND and, would provide the best source of information. As the Waitemata DHB catchment area covers both the North Shore and the Waitakere hospitals why is the study not being run from the Waitakere Hospital? Compared to the North Shore, the Waitakere population is more diverse and has more people from low school deciles. The Committee understands that there may be implications around health literacy and how you explain the study but wanted to know why Waitakere Hospital is not a focus of the study.
4. The Researcher(s) explained it is because Waitakere Hospital does not have house officers and registrars and that the study is just not feasible. If it does prove to work they will carry it out at Waitakere. This is essentially the pilot study.
5. The Researcher(s) confirmed that Maori consultation was made with Helen Wihongi of Waitemata DHB.

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 there should be a linking document where identifying information is coded and the code is kept in the database. The coded information and the code are physically separated. In this way the information is potentially identifiable (Ethical Guidelines for Intervention Studies, paragraph 7.2)
2. The Committee recommended that the hard copy of the study data is locked away in a filing cabinet and the study data’s electronic copies are kept password protected hospital computer.
3. The Committee requested that Hamish Neeve’s sample size calculations be reviewed as it seems incorrect (ie, “430 in each arm”).
4. The Committee asked that a written debrief document is prepared. Demonstrate the gap to them which should help with acceptance of the research.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (Participant Information Sheet/Consent Form (PIS/CF):

1. The Committee requested that participants are told they can withdraw their data if they would like to and it will not compromise the relationship between the community and the investigators and the research. Please state this in the PIS and protocol
2. Please include HDEC’s standard compensation statement (for non-commercially sponsored intervention studies) as follows:

If you were injured in this study, 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 ensure study data confidentiality is protected (Ethical Guidelines for Intervention Studies, para 7.2)
* 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 review the sample size calculations as scientific soundness is ethically important (Ethical Guidelines for Intervention Studies, para 5.5)

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

|  |  |  |
| --- | --- | --- |
| **6.** | **Ethics ref:** | **18/NTB/161** |
|  | Title: | Ketone monoester supplementation in individuals with pre-diabetes |
|  | Principal Investigator: | A/Professor Max Petrov |
|  | Sponsor: | The University of Auckland |
|  | Clock Start Date: | 20 September 2018 |

Professor Max Petrov (CI) was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of ethical issues (resolved)

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

1. The Researcher stated that he was undertaking this study to better understand the physiology of blood/glucose control and how it may have future implications on preventing diabetes. This is still a relatively new area as only two other similar physiological studies that have been conducted and published so far.
2. The Committee asked if HVMN and Boost are available over the counter in NZ.
3. The Researcher responded that they are only commercially available from the States and can be bought on line.
4. The Committee questioned how participants will be recruited.
5. The Researcher explained that they would use an application called Maybelee to advertise the study. The research team have used this application in some of their other studies to recruit health volunteers. They would also use posters and word of mouth.
6. The Committee questioned if the study is likely to obtain abnormal blood results from testing.
7. The Researcher stated presence of diabetes will be an exclusion criteria but if it happens that they uncover incidental findings of diabetes, they will inform participants. The studies goal is to include only those who have not reached the diabetes threshold.
8. The Committee asked whether individuals who are pre-diabetic will know that they have this condition.
9. The Researcher stated in New Zealand only half of patients who have diabetes are not aware of the subtle changes of blood/glucose control. The Researcher estimates that 40-50% of individuals will not know that they have pre-diabetes.
10. The Committee questioned this the recruitment advertisement is aimed at pre-diabetics.
11. The Researcher responded that some individuals know that there are factors that pre-dispose abnormal glucose metabolism such as lack of physical activity, high weight and family history. The research team will therefore need to screen to see if blood/glucose level is in the pre-diabetes range.
12. The Committee stated if people that come in for screening end up being withdrawn as a result of the process then this should be made clearer in the exclusion and inclusion criteria details.
13. The Committee were unclear as to what group of people would make up the study population as study documents suggest that both normal healthy and pre-diabetic participants will be recruited. Is this the case because the study will take all that respond to the advertisements who think they might be pre-diabetic and then screen by telephone?
14. The Researcher advised that screening by telephone is to save time and, before participants are assigned to placebo or intervention, their blood/glucose readings will be made. Only those in the pre-diabetic range will be included.
15. The Committee questioned if any interim reviews of result will be carried out during the study and whether the study would carry on if no differences were found between the two groups.
16. The Researcher replied that the study is a pilot and it is already quite limited with 30 participants. It has study power to detect change in blood/glucose control. The Researcher felt that given the limited sample size an interim analysis may not be essential.
17. The Committee commented that the drink has a distinct bitter taste and questioned whether the research team are confident that it can be disguised with Estevia.
18. The Researcher confirmed that it can. This is based on two previous Oxford published studies that used the same method as this study. The research team also receive advice on the placebo design from Auckland University’s Pharmacology Department.
19. The Committee noted the peer review mentions “very careful review of medication” for pre-diabetic population and questioned if this implies those already on glucose lowering medication or in general.
20. The Researcher replied that he is unsure but to keep in mind that the study is a RCT so even if there is bias in terms of medication that individuals perceive, it will likely be evenly distributed between the groups so he did not think medication will skew the study results.
21. The Committee questioned if participants would be on corticosteroids as if there are 30 participants then it would be possible to skew results. (eg, 5 people on medication in one arm) The Committee advised that it would be worth recording and then looking over afterwards. The Committee noted that variable as baseline are seen sometimes, even in RCTs.
22. The Researcher confirmed that he will consider this advice and implement it.

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 supply the participant recruiting poster for HDEC to review. This needs to be viewed before a final decision can made.
2. The Committee stated that the Standing Committee on Therapeutic Trial (SCOTT) may have to review this study as it is unclear whether it involves a nutritional supplement or therapeutic trial. Please contact MEDSAFE for clarification and inform HDECs of the outcome.
3. The Committee commented that the burden of disease in Maori and Pasifika people is disproportionately high and as such Maori should be included in the study. Please target the advertisement to aid this goal and conduct Maori consultation as part of locality authorisation which you can do through the assistance of your research office.
4. The Researcher responded that some individuals know that there are factors that pre-dispose abnormal glucose metabolism such as lack of physical activity, high weight and family history. The research team will therefore need to screen to see if blood/glucose level is in the pre-diabetes range.
5. The Committee stated if people that come in for screening end up being withdrawn as a result of the process then this should be made clearer in the exclusion and inclusion criteria details.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (Participant Information Sheet/Consent Form (PIS/CF):

1. The Researcher confirmed that in the initial screening visit consent would sought, blood test made and participants made away that they need to come back fasted for the intervention. Please ensure this is clear in the PIS/CF.
2. The following have been mentioned but are not included in the PIS/CF and need to be:
3. Explain the 24 hour food log
4. Explain that participants are required to note the exact diet they’ve consumed the day before the 2nd testing visit
5. The supplement drink and the following meal drink
6. Detail of the randomised cross over design with placebo. It should clarify what happens to the abdomen sensor. Please clarify if it is removed at end of second visit.
7. What happens if a participant withdraws before their second first (ie, would they wander around with the sensor in their stomach?)
8. Please clarify if this study is for an academic qualification.
9. Include a sensor picture with its location in the body to aid participant understanding.
10. Include that a cannulation will be used.
11. The Committee noted that they are a few terms that are quite medical for example, post nutrient stimulation, impacts on glycaemic response. Please use more lay language.
12. Remove the ethnicity option from the Consent Form, this can be collected in the questionnaire document.

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)
* Please provide a copy of the recruiting advertisement so the Committee can review it for ethical appropriateness (Ethical Guidelines for Intervention Studies, section 6).
* The Committee stated that the Standing Committee on Therapeutic Trial (SCOTT) may have to review this study as it is unclear whether it involves a nutritional supplement or therapeutic trial. Please contact MEDSAFE for clarification and inform HDECs of the outcome (Ethical Guidelines for Intervention Studies, Appendix1)
* The Committee commented that the burden of disease in Maori and Pasifika people is disproportionately high and as such Maori should be included in the study. Please target the advertisement to aid this goal and conduct Maori consultation as part of locality authorisation which you can do through the assistance of your research office (Ethical Guidelines for Intervention Studies, para 4.7-4.10)

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

|  |  |  |  |
| --- | --- | --- | --- |
| **7.** | **Ethics ref:** | **18/NTB/164** |  |
|  | Title: | A randomised double blind placebo control trial of the efficacy of oral N-acetyl Cysteine in mild traumatic brain injury patients presenting to a regional Emergency Department |  |
|  | Principal Investigator: | Dr Tom Jerram |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 20 September 2018 |  |

Dr Tom Jerram (CI), Andrew Munroe and Mark Goodenstyner were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of ethical issues (resolved)

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

1. The Committee questioned the timing of recruitment and whether those being recruited would really be consentable as they would have had a knock to the head.
2. The Researcher(s) replied that essentially participants need to be consentable. One of the study’s inclusion criteria is clinicians should be confident that participants can competently give consent. The Researcher(s) felt that making this judgement during the study should be straightforward as this a process they deal with regularly in standard of care situations.
3. The Committee questioned if participants would be taking medication there and then.
4. The Researcher(s) replied that in the original study there was a 72 Hour window and the group that received meds in 24 hours had a better outcome though the later group still benefitted.
5. The Committee queried where: (a) consent would take place, (b) the Participant Information Sheet (PIS) would be read and how long participants would have to read it. The Committee also wanted to know who would go over the PIS with participants.
6. The Researcher(s) stated that participants would be provided with a cubicle for privacy. Potential participants would be identified by RMOs who would then notify the research team. An ED consultant or nurse practitioner would then evaluate those identified for competence to consent.
7. The Researcher(s) confirmed that the proximity of symptoms to the consent process will vary as they could have people who present as really confused and non-consentable to those who hit their heads two days prior and just have ongoing headache and dizziness. How close this proximity is, will be something they will have to be careful of.
8. The Committee questioned the length of time given for consent until participants leave the cubicles. Will a time limit be set for the use of the cubicles?
9. The Researcher(s) stated they will give participants as long as they need to make a decision. There will be other spaces they can go to, to consider their options, either near the ED or within the ED. If participants show up a day or two later they will have alternate spaces available.
10. The Committee queried if seeking consent will be done as the last thing before participants go home or will it be done while they are being observed to see if their level of consciousness is going down and they might need further treatment. Will consent be offered to participants once they have been signed off as fit to go home?

1. The Researcher(s) responded that the offer for consent would only be made once participants have been clearly identified to have injury/symptoms/signs consistent with concussion. Consent would therefore be offered anytime during ED encounter or right up to the last thing they do with participants before they go home.
2. The Committee asked how the research team would know that participants are consentable as no test is being used. The Committee wanted the research team to consider, given this is research that there is a lot to be read and understood and not much time from being informed to consenting.
3. The Committee reminded the Researcher(s) that there is a difference in consenting for clinical treatment and consenting for research. The Committee suggested that consent can be the last thing the research team does once participants have been signed off as okay to go home and take care of themselves.
4. The Researcher(s) stated the study is set up in such a way that participants can go away to consider their options and if they want to be part of the study, they can return and have the initial dose. Also if they find themselves consenting at any stage during the subsequent 7 days they can withdraw their consent.
5. The Committee questioned if for the 72 hour time window, participants could be given information as they go home and get them back the next day to consent.
6. The Researcher(s) confirmed this could be done but there were issues to be considered;

i) in the original RCT; there is a falloff in efficacy in the first 24 hours and patients lose a portion of potential benefits

ii) No guarantee that delay in 24 hours will change their ability to consent, concussion is a really complex phenomenon and often cognition will be fine. The way that concussion affects the brain is still not understood. They are not sure that giving them anymore time would guarantee a better consent ability then if it was sought the day before.

1. The Committee asked if preference could be made for people that have family support with them to help with decision making.
2. The Researcher(s) noted this as a reasonable suggestion. They would add this to their inclusion criteria
3. The Committee emphasised that participants should still make the decision for themselves but with whanau there for support.
4. The Researcher(s) confirmed that Metagenics would not receive any of the study data: Metagenics is not the study sponsor nor is it involved in any of study design.
5. The Committee requested details on the randomisation that Metagenics will use in the protocol to find out whether it is block and to make sure it is as tamper proof as possible.
6. The Committee wanted to know whether there will be a difference in taste between placebo and N-acetyl Cysteine. Could participants make this distinction?
7. The Researcher(s) replied according to Metagenics chemists participants will not be able to tell a difference in taste in the products.
8. The Committee stated because the study’s primary outcome is highly subjective it is really important that participants are blinded and to strengthen study, it would be good to ask at final visit what product participants thought they received.
9. The Committee queried if refunds will be given for transport as participants will be attending 3 follow up visits which are beyond standard of care.
10. The Researcher(s) responded in Nelson participants can park for free. The study can provide taxi chits for those on hardship. The study is set up to offer a visit back to hospital but if it can provide most of the primary and secondary outcome via participants’ SMART phone, which will minimise a lot of people coming back to hospital then, they will consider this.
11. The Committee noted that this will mean a change in conduct of study therefore a change in protocol. HDEC will need to review this so please submit this change in a post approval-amendment submission once the study has HDEC approval.
12. The Researcher(s) stated an issue of concern is the follow up rate. They believe that 40% of the treatment arm are asymptomatic at 7 days so a lot of people will not come back because they feel better. They thought this would be a better way to capture data fully.
13. The Committee questioned if the Braincheck approach is an IPAD based assessment and if involves an assessment of competent ability.
14. The Researcher(s) responded that it can accessed via IPAD, SmartPhone, PC or Mac.

Braincheck is essentially several well validated neurocognitive tests that take between 5-10 minutes to complete. It tests executive function and processing speed of memory and cognition which individual can carry out themselves. The tests do not provide a measure of capacity and it will not give the patients baseline.

1. The Researcher(s) asked if participant records can be linked to Otago University’s RED CAP database
2. The Committee stated this would not be acceptable.
3. The Committee questioned if Nurse practitioners take consent for surgery and therapeutic interventions and if they do not then they should not take consent for this research. The Committee felt that only ED doctors should take consent for this research because of the necessity to evaluate capacity clinically.
4. The Researcher(s) agreed and advised that senior registrars will attend to consent so that they make the decision about competence.

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 if preference could be made for people that have family support with them to help with decision making.
2. The Researcher(s) noted this as a reasonable suggestion. They would add this to their inclusion criteria
3. The Committee emphasised that participants should still make the decision for themselves but with whanau there for support.

Please include this point in both the protocol and participant information sheet.

1. The Researcher(s) advised the study is set up to offer a visit back to hospital but if it can provide most of the primary and secondary outcome via participants’ SMART phone, which will minimise a lot of people coming back to hospital then they will consider this.
2. The Committee noted that this will mean a change in conduct of study therefore a change in the protocol. HDEC will need to review this so please submit this change in protocol as post approval-amendment submission once the study has HDEC approval. Please include all supporting documents (in their tracked changes versions) affected by this change.
3. The Committee questioned if Nurse practitioners take consent for surgery and therapeutic interventions and if they do not then they should not take consent for research. The Committee felt that only ED doctors should take consent for this research because of the necessity to evaluate capacity clinically.
4. The Researcher(s) agreed and advised that senior registrars will attend to consent so that they make the decision about competence. Please record this in both the protocol and the participant information sheet.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (Participant Information Sheet/Consent Form (PIS/CF):

1. The Committee reminded the research team that HDECs don’t endorse research. Please state that the study was approved by the Northern B HDEC and provide the HDEC reference number.
2. Please inform participants of the further visits at 1 month and at 6 months if symptoms persist.
3. Please be clear that data will be taken from tests done as well as from participant records.
4. The Committee noted that N-acetyl Cysteine’s intravenous and oral preparations have been confused. Please distinguish these preparations when you discuss their uses, doses and side effects. Please provide frequency data to the side effects, particularly nausea and vomiting as they are side effects of concussion as well.
5. Please clearly explain how individuals can sort out what their side effects are due to.
6. Please code study data so it is de-identified. Individual data is allocated a study ID with a separate linking document containing all identifiers.

.

Decision

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

* Please ensure participants have family/whanau support with them to assist with decision making. Participants should still make the decision for themselves with whanau there for support (Ethical Guidelines for Intervention Studies, para 5.33)
* Please amend the study protocol taking into account the suggestions made by the Committee (Ethical Guidelines for Intervention Studies, para 5.41)
* 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 Mr John Hancock and Dr Nora Lynch.

## General business

1. The Chair reminded the Committee of the date and time of its next scheduled meeting, namely:

|  |  |
| --- | --- |
| **Meeting date:** | 06 November 2018, 12:00 PM |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Road East, Ellerslie, Auckland |

The following members tendered apologies for this meeting.

* Mrs Leesa Russell and Mrs Maliaga Erick

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 4.05pm.