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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 12 April 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 | Confirmation of minutes of meeting of 08 March 2016 |
| 1:30pm | New applications (see over for details) |
|  | i 16/NTA/33  ii 16/NTA/34  iii 16/NTA/35  iv 16/NTA/36  v 16/NTA/38  vi 16/NTA/40  vii 16/NTA/42  viii 16/NTA/44 |
| 4:50-5:15pm | Substantial amendments (see over for details) |
|  | i 15/NTA/146/AM01 |
| 5:15pm | General business:   * Noting section of agenda |
| 5.20pm | 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 |
| Ms Susan Buckland | Lay (consumer/community perspectives) | 11/11/2015 | 11/11/2016 | Present |
| Dr Karen Bartholomew | Non-lay (intervention studies) | 01/07/2013 | 01/07/2016 | Present |
| Dr Christine Crooks | Non-lay (intervention studies) | 11/11/2015 | 11/11/2018 | Present |
| Ms Shamim Chagani | Non-lay (health/disability service provision) | 11/11/2015 | 11/11/2016 | Present |
| Dr Kate Parker | Lay (consumer/community perspectives) | 11/11/2015 | 11/11/2018 | Present |
| Dr Charis Brown | Non-lay (intervention studies) | 11/11/2015 | 11/11/2018 | Present |
| Ms Rosemary Abbott | Lay (the law) | 15/03/2016 | 15/03/2019 | Present |

## Welcome

The Chair opened the meeting at 1:00pm and welcomed Committee members.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

## Confirmation of previous minutes

The minutes of the meeting of 8 March 2016 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **16/NTA/33** |
|  | Title: | Top up 4 yr top up. Waikato Rangatahi Rheumatic Heart Disease Secondary Prevention Study. |
|  | Principal Investigator: | Prof John Oetzel |
|  | Sponsor: | Waikato DHB |
|  | Clock Start Date: | 31 March 2016 |

Prof John Oetzel 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.

Dr Charis Brown declared a potential conflict of interest. The Committee agreed to allow her to remain in the meeting room and take a full part in the discussion and decision relating to that item of business.

Summary of the study

1. This study will aim to incentivise compliance with recommended care (monthly benzathene injections) for young people with rheumatic fever. The intervention is a physical phone and free monthly texting (top up) with injection compliance. The researchers plan to do multiple baselines to see whether the intervention effects change over the long term. The researchers are looking for ways to help improve life for this vulnerable group and this incentives intervention was an idea generated by young medical students in the region as a relevant intervention for the target group.
2. The committee asked why the researchers have chosen cell phones vs other incentives eg voucher. The researchers stated that talking to youth in the community about what is beneficial showed that cell phones are something that they use every day and they then created an app that connects with this group and gives them information they may not otherwise have.

Summary of ethical issues discussed:

1. Peer review suggested not all detail was provided in the protocol. No detail about recruitment or what the plan would be if recruitment to the study is poor ie if the current non-compliant youth aren’t contactable by the district nurses how would the offer of the intervention be made? The committee also queried what data is being recorded (access to medical records or new data) and data on intervention acceptability. The committee requested an updated Protocol addressing these issues be provided, and the responses included in the PIS where relevant.
2. The researchers are working with district nurses to identify and contact people who are non-compliant. Contact will be by letter and phone contact to see if those identified are interested in participating and they would not force compliance if people are not interested in being in this study. Contact alone might prompt them to come back and have injections without having to offer the incentive.
3. In terms of scientific validity of the study, the committee queried how the researchers would determine current cell phone ownership/use. How will the researchers determine the effectiveness of the cell phone vs the text top up incentive. Could the participants receive a text top up on their regular phone? How would this data be captured? The committee requested that the researcher(s) consider this in their revised Protocol.
4. The texting programme is funded for one year. The researchers would like to seek additional funding to track and see progression with regular support from district nurses. If successful it would be good to have this incentive strategy institutionalised become business as usual.
5. In terms of the data recording the researchers explained that district nurses will develop a chart (or record from current records) which states information including how many times they have contacted a person and any medicines not taken. The researcher stated that the district nurses will collect the data and the data will be then anonymised for analysis. However the Committee noted that a co-investigator currently has access to medical records and therefore may view identifiable records. The Committee requested that clarification of what data is collected, by whom, and who will view identifiable data is included in the revised Protocol.
6. The researcher stated that they will not have access to identifiable data used to determine eligibility for the intervention (the local rheumatic fever register), however the Committee noted again that a member of the research team already has this access. The Committee requested clarification on this issue in the revised Protocol. If the researchers do wish to access the register then they need to seek and be granted appropriate permissions as a research group.
7. Data collection and access needs to be made clear on the PIS as well.
8. The committee would like clarification about the research team members, for example, is the project manager part of the research team or an external person? Specification of who will have access to identifiable patient information at what points should be included. Please note that contact details are considered health information under the Health Information Privacy Code and that researchers cannot access this data prior to patient consent.
9. The committee noted that the researchers had stated that the study is Kaupapa Mãori Theory based. The researchers stated that what they were trying to express is that by working with advisory group and including youth and emphasising Tino rangatiratanga as opposed to having researchers do something to them. The committee recommended for future reference that maybe use the term ‘Maori centred’ could have been used instead.
10. The committee noted that cell phones had the potential for misuse e.g. cyberbullying, pornography etc. and also the potential for participants to remove the rheumatic fever applications or to lose the phone. While these are methodological considerations the management of issues such as these would be beneficial in terms of a revised Protocol and PIS.

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

1. Please provide an updated Protocol addressing the issues outlined above – patient recruitment processes, data access and recording, research team and identifiable data, additional information collection process, consideration of potential misuse issues.
2. Please review the information sheets and consent forms for any typos and also with a view to checking that all information is clear to make sure that anyone who reads it will understand. For example, the ‘What will my participation in this study involve?’ section doesn’t explain how or when the participants will get a cell phone.
3. Consent form: please include yes/no options for statements that are truly optional. In this case, receipt of a summary of study results is the only optional statement.
4. Please review the parental information sheet and consent form to check that reference to you/your child is consistent (i.e. written from parents’ perspective).
5. Information sheet, 14-16 year olds: page 3, ‘What happens after the study or if I change my mind?’: Please include that the health information must be stored for 10 years after the participant reaches the age of 16.

Decision

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

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

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

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| **2** | **Ethics ref:** | **16/NTA/34** |
|  | Title: | SOF/VEL Peri-Operative Transplant |
|  | Principal Investigator: | Prof Ed Gane |
|  | Sponsor: | Gilead Sciences, Australia & New Zealand |
|  | Clock Start Date: | 31 March 2016 |

Ms Amy Cole was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of the study

1. HCV is the leading indication for liver transplantation around the world including here in New Zealand. Following liver transplantation for HCV cirrhosis, recurrent infection of the graft is universal and leads to rapid fibrosis and progression to cirrhosis and graft failure in 10-20% of patients. As a result, the outcomes following liver transplantation for HCV cirrhosis are the worst of all indications.
2. Current interferon based therapies are contraindicated at this time because of the high risk of causing rejection. This current study, the first of its kind in the world, will look at whether a short course of SOF/VEL FDC, immediately post-transplant when the virus is at its lowest level, will prevent recurrent HCV infection of the graft.
3. This study will enrol 10 participants from the New Zealand Liver Transplant unit and test the safety and efficacy of two potent antiviral drugs in participants with chronic Hep C virus following liver transplantation. The treatment will start on day 1 following transplantation and the primary objective is to assess the proportion of participants who remain clear of chronic Hep C 12 weeks after completing the short course (4 weeks) of treatment.
4. Current interferon and ribavirin-based regimens have poor tolerability and efficacy before and after transplantation. This study drug is not metabolised by the liver and has no significant drug-drug interactions and has high efficacy in non-transplant populations.

Summary of ethical issues discussed:

1. The committee asked whether the phase I trial was done in a transplant setting. The researcher confirmed that it was. The committee queried whether there were any issues involved specific to transplant and the researcher advised that there were no known additional risk issues.
2. Serious Adverse Events will be monitored by an internal data safety monitoring committee. It will be set up with Gilead Drug Safety and Public health. The DMC is described on page 69 of the protocol whereby an interim review will occur after the first five participants have completed the study period. A formal process will be put in place after first five patients and the researchers will not progress with the study if there are any safety concerns identified in the first five participants.

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

1. The committee noted that there are three optional sub study information sheets and consent forms: optional pharmacogenomics research, optional testing of explanted liver an optional blood sample collection for future research and queried whether the pharmacogenomics sub-study could be combined with the blood sample collection for future research. The researcher explained that the pharmacogenomics study will require an additional blood test and the blood sample for the FUR will already have been taken. They had looked at whether it was possible to combine the three sub-studies within one information sheet but had decided to add a visual check box on page 5 of the main information sheet.
2. The committee noted that some people will have a view about tissue going overseas but not same view about blood going overseas so it will be good for the researchers to separate this out. The committee noted the importance of the researchers being clear about when genetic testing being done or proposed in future research.
3. Page 13: The committee noted the statement at the top of this page – “Your coded study information and samples may also be used for additional unanticipated medical and/or scientific research projects in the future relating to the development of the study drug” seems to imply future unspecified research in the main PIS, and noted that this information should be kept with the information for future unspecified research if it does related to this.

Decision

This application was *approved* by consensus.

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| **3** | **Ethics ref:** | **16/NTA/35** |
|  | Title: | Percutaneous cannulation of the thoracic duct |
|  | Principal Investigator: | Professor John Windsor |
|  | Sponsor: | The University of Auckland |
|  | Clock Start Date: | 31 March 2016 |

Dr Alistair Escott and Mr Scott Aitken 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.

Dr Kate Parker declared a potential conflict of interest, and the Committee agreed that it would allow her to remain in the room for the discussion and decision making for this item of business.

Summary of the study

1. This study involves a stepwise approach for three related projects for a new surgical intervention. The first two parts will involve patients and the third part will be laboratory based.
2. Project 1 will used a lymphangiography to demonstrate the thoracic duct anatomy. The researchers will minimise the use of radiation and will aim work out the timing of when it will be best to do the cannulation. If successful they will use the technique to provide a road map to develop the technique of peripheral transvenous cannulation (PTCTD).
3. Project 2 will use the PTCTD to sample thoracic duct lymph and divert thoracic duct lymph flow.
4. There are potential advantages in draining lymph in this way (reducing the severity of pancreatitis); this technique if successful is less invasive than an open method. The current gold standard for accessing the thoracic duct is open surgical cannulation, a method developed over 60 years ago. The technique to be trialled is a minimally invasive percutaneous method and if successful would be an improvement in the current method of open surgical cannulation.
5. This study is a follow up to a previous study (12/NTB/67) looking at duct embolization, which encountered some problems in the early stage of the project and was halted. This study aims to minimise the risks of embolization. The committee requested that the research team update the committee after each project either as part of the annual progress report or by submitting a post approval form as an amendment via Online Forms. Patients in project 2 also have the potential to benefit from lymph drainage.

Summary of ethical issues discussed:

1. The committee noted that on reading the high quality peer review they are satisfied that safety issues have been addressed. In terms of data safety it was noted that the investigators will need to consider alternative options for independent monitoring if HRC funding is not forthcoming. The researchers noted that in that event they would progress slowly and also establish a committee through the ADHB.
2. The committee queried what the researchers intend to do if project one is not successful. The researchers explained that plan B would be to study alternatives and they would apply to the committee for ethical approval.
3. The committee noted that pancreatitis patients may be very unwell or potentially alcoholic (have impaired competence for consent). The researchers explained that they will not consent seriously unwell patients (e.g. in ICU) these patients are specifically included. This patient cohort will be made up of those with moderate systemic inflammation response. The researchers will only consent those who are able to consent for themselves.

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

1. Project 2 Information Sheet: ‘What will happen to my tissue samples?’ The researchers confirmed that tissue samples may go overseas to Monash University for testing with equipment that is not currently available in their laboratory. The committee advised consideration of the following standard statement regarding cultural issues involved for Mãori in sending tissue overseas: *You may hold beliefs about a sacred and shared value of all or any tissue samples removed. The cultural issues associated with sending your samples overseas and/or storing your tissue should be discussed with your family/whanau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult prior to participation in research where this occurs. However, it is acknowledged that individuals have the right to choose.”*
2. Project 2 Information Sheet: ‘What are the possible benefits and risks to you of participating?’ Please include the risks of bleeding and sepsis/infection (standard intervention risks). Both were identified in the study protocol.
3. Please state that ethical approval is from the Northern A Health and Disability Ethics Committee.

Decision

This application was *approved* by consensus.

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| **4** | **Ethics ref:** | **16/NTA/36** |
|  | Title: | Primary Prevention of Stroke in the Community |
|  | Principal Investigator: | Prof Valery Feigin |
|  | Sponsor: | AUT |
|  | Clock Start Date: | 31 March 2016 |

Professor Feigin and Dr Rita Krishnamurthi were present in person for discussion of this application.

Potential conflicts of interest

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

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

Summary of the study

1. This study aims to recruit 320 people who are registered patients of Auckland PHO practices who have an estimated five year risk of cardiovascular disease of 10% or more. Health and well-being questionnaires will be given at 3, 6, 9 and 12 months and risk of stroke will be assessed at 9 months by a participant’s GP. Participants will be randomised to Health and Wellness coaching with usual care.
2. Potential participants will be identified primarily via Nirvana Health Group, who manages the largest network of primary health care clinics in New Zealand. Eligible participants will be sent a text message from the PHO informing them of the study. Note to researcher: the text message is very brief and should inform the person that if they reply ‘Yes’ then Nirvana will be supplying their name, contact details (home and/or mobile contact numbers) to the researchers. Please amend.
3. Once this consent is received to contact participants the researchers will phone potential participants to let them know what the study involves and if interested they will send out the information sheets and consent forms. Participants will be screened at this point.
4. If eligible, PIS and CF will be sent to the possible participant. After signed consent forms are received the participants will be enrolled in the study. Participants will then have a screening assessment that will include a standardised screening questionnaire and eligible participants will be randomised into HWC or usual care groups. If the individual contacted says that they are interested in being contacted about the study a second round of screening involves the use of PHQ-9 mood questionnaire. The committee noted that a screening tool is suggestive of risk. If the score suggests that someone is at risk of harm then the researchers should exclude them from the study and tell the person’s GP. The committee noted that this might apply to hazardous alcohol use as well. The committee would like to see the script for this conversation.
5. The researchers queried when they should get consent from the participants – before or after screening. The committee asked that the researchers seek verbal consent *before* the screening when they call the potential participant and that the research team make sure that the verbal consent is carefully and completely documented.

Summary of ethical issues discussed:

1. The committee had some questions about how the researchers intend to do the assessments: the committee noted that GP’s will be involved at 9 months doing a follow up assessment and that the assessment is paid for from the study budget. The payment to GP and PHO is 100 dollars Koha for every patient randomised. The researchers explained that the payment will cover the cost of a GP doing screening and for the PHO to find the people they need according to the criteria. In other words they are being employed on behalf of the researchers.
2. The committee queried the method of recruitment script noting that need for a careful approach about the content when contacting patients by text. The patients would have known from blood and other tests that they are in a risk category and that researchers explained that the text message will not say anything about risk. It will simply mention the study and will ask whether they are interested about finding out more about it.
3. The committee asked whether the researchers were aware whether the pacific island communities would have the same access to this method (texting), of recruitment and noted the need to make sure that those in higher risk groups have equal access to the study. The researchers noted that another method of recruitment is to run information evenings and ask for interest there rather than through text message alone.
4. Information stated in the study protocol around statistical considerations and power calculations is that an intentions to treat analysis will be employed and that 320 participants (80 Mãori, 80 Pasifika, 80 Asian and 80 NZ European) in that order. The committee queried whether the researchers were expecting pre-stroke to be in that order. It is irrelevant and all will be equally powered.
5. The research team have also consulted with Pacific Island people and have a Pacific Island person in the team advisory group. One of the lead investigators is Asian and is using her own knowledge. The researchers have consulted more widely with TANI and people in community networks and used radio advertising to increase awareness. The study design is rare in that it aims to get the same numbers of people from different ethnic groups. Hine Elder who is in the advisory group noted that this is one of few studies that is powered to look at ethnic differences. The committee would like to see information about how the power and recruitment processes are going in any annual progress reports submitted for this application.
6. The committee queried whether the interventions is this study are borrowed or designed. The researchers confirmed that they are standard psychological intervention/model and as such there has been no cultural consultation into their design specific to this study.
7. The committee noted that the researchers have touched on cultural issues for Mãori and noted that some Mãori may not be comfortable with phone interviews and prefer face to face contact. The committee asked how the researchers intend to assess this. The researchers stated that they will ask participants what they prefer and it they would rather not interview by phone then they can meet face to face.
8. The committee queried whether there had been any concerns expressed by the Pacific Island community. The researchers stated not in terms of this intervention. Advice received about recruitment was to get into the community and talk rather than cold call. The committee saw no problems with the size of the group they wish to recruit and that the recruitment criteria is not exclusive. It did express concern about possible exclusion of “high needs” pacific peoples who cannot speak English and advised that if the researchers haven’t dealt with how to include this group already that they consider seeking advice from their pacific advisory group to support them.
9. The researchers confirmed that the study received independent scientific peer review from the National Science Challenge.
10. The committee asked how the researchers will account for participants who are receiving other interventions in their assessments. They have talked and PHO meetings about excluding people who are receiving other types of intervention once they have talked with them. If a person involved in the trial is exposed to other interventions that are not experimental, the researchers will record the interventions. Will include in flow chart and ask to include. Please update this in your protocol and provide the committee with the updated protocol.

*Additional summary of ethical issues discussed following the meeting by teleconference on 28 April 2014:*

1. The Chair, Dr Christine Crooks and the HDEC secretariat met with members of the research team by teleconference to further discuss and clarify a couple of points that the committee had about the research team’s access to health information and the protection of peoples’ privacy.
2. The researchers confirmed that the Nirvana information system will send text messages to potential participants and the committee noted that the text message it had viewed as part of this application is brief and should include more detail about what information will be released to researchers if a person indicates ‘yes’ that they would be interested in receiving more information about the study. The text message should indicate that a person’s name, and specific contact details will be sent to the researchers.
3. The researchers explained that they had earlier today met with Nirvana who had suggested a text change to include that they will provide AUT with contact information and the research team can add the detailed information about what contact information will be released in that text. The committee was satisfied with this and noted it is important that people know from the start what information they are consenting to be released.
4. The researchers confirmed for the committee that part 2 of the process will involve the researcher phoning the potential participant (individuals who have responded ‘yes’ to the text message), and if they are interested the researchers will send them information about the study. There will be two rounds of screening – the first will be for potential participants to answer a set of inclusion/exclusion screening questions and then once the participants have provided written consent after considering the participant information sheet, they will be asked to complete the PHQ-9 mood questionnaire.
5. The committee asked that the researchers be more transparent with the potential participants at this stage and inform them that they may or may not be eligible to enter the study.
6. The researchers explained that they will clarify at the first phone call that they will introduce themselves and the study and not that participants may or may not be eligible and will send the PIS/CF out in an email. Once the participants have received them they will make contact again with the screening questions.
7. The committee asked whether at first contact it is necessary for the researchers to have received the NHI. The researchers clarified that they won’t receive the NHI numbers until a person has consented to being in the study. They will make this change in the protocol.
8. The committee checked its understanding that after the screening then the researchers will be given access to health information form Nirvana. The researchers confirmed this to be the case and the committee queried again whether NHI numbers were therefore needed? The researchers explained that they will not use NHIs to access any information and that they will be used as a “double-check” to confirm participant identity. The provider has a spreadsheet that is pre-populated with the data they need and this is the only information that the researchers will receive.
9. The committee asked that the researchers change the wording in the participant information sheet to state that they are only accessing information indirectly from the health care provider and suggested the following statement: *“The following information about you will be forwarded to the research team by Nirvana.”*

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

1. 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) please state.
2. Please describe how confidentiality of health information will be protected from first contact.

Decision

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

* Please amend the information sheets and consent forms, taking into account the suggestions made by the committee *(Ethical Guidelines for Intervention Studies, para 6.22)*
* Flow chart. Please update this in your protocol and provide the committee with the updated protocol that satisfies regulatory privacy issues.

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

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| **5** | **Ethics ref:** | **16/NTA/38** |
|  | Title: | Probiotics & Prebiotics in Prediabetes |
|  | Principal Investigator: | Ms Christine Barthow |
|  | Sponsor: |  |
|  | Clock Start Date: | 31 March 2016 |

Ms Christine Barthow and Dr Kristin Wickens 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 study is a pilot study that aims to inform the progression from pre-diabetes to type II diabetes. It is hoped that this study will lead to a larger intervention study. There is evidence that probiotics reduce diabetes in pregnant women. Apart from lifestyle and dietary advice, there is no therapeutic remedy, hence the trial with prebiotics, probiotics and placebo.
2. The researchers aim to recruit 90 participants, 30 in each arm as this is the best the researchers can estimate to see effect size in the results.

Summary of ethical issues discussed

1. The committee noted that the researchers will use an internal data safety monitoring committee to monitor any serious adverse events and that this arrangement seems sufficient for this study. The researchers explained that they have worked with this probiotic in the past including in intervention studies in early pregnancy and infants in their first two years of life and have studied more than 400 people in the field without any safety concerns.
2. The committee noted that peer review submitted was done well but that the reviewer was also an investigator in the study. The study has also been peer reviewed by the University of Otago research committee who awarded the research team a grant. The committee would like to see what the research committee said in its peer review.

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

1. Page 3, ‘What will my participation in the study involve?’: the committee noted that the researchers might wish to add examples of other ingredients that participants could use to add to their cereal. For example, people might want to put fruit with the cereal.
2. Page 4, ‘What if something goes wrong?’: please remove the current statement and replace it with the following: *If you were injured in this study, which is unlikely, you would be eligible* ***to apply*** *for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery.  
     
   If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.*
3. The committee noted that the consent form identifies that stool samples will be sent overseas and the information sheet states what happens after in that fecal samples will be analysed in NZ or overseas. The researchers explained that there will be two possible uses of the samples: one is to do sequencing to identify type and abundance of various bacteria in stool samples. The other is to look at a metabolic analysis of fingerprint that gut bacteria leaves behind in stool samples. The tests are expensive so the researchers are considering where it will be best where to send and get relevant analyses done. Please give a brief account of this in the FUR information sheet and consent forms. Please include more information on the types of tests you will do if the samples go overseas and include that they are genetic as participants won’t know what sequencing is.
4. Please make clear in the FUR participant information sheet and consent forms whether participants can withdraw consent and get their samples back, whether you will keep the samples identifiable.
5. The researchers confirmed that the tissue bank is an already established umbrella tissue bank that other studies sit under. This will be a study specific collection under that umbrella tissue bank. Yes/No questions in the consent forms have given options in same areas of current research or research that is currently approved. People can choose which ones they are consenting to. The researchers confirmed that the options given to participants were real and that their tracking allowed participants to have these selections annotated to their records.
6. The committee noted the comment in the peer review document that there is a comment about an element of concealment in this pilot study in relation to the two cereal interventions (prebiotic). The researchers believe that this element is justified by scientific validity and that the study would be difficult to do otherwise. The committee asked whether the researchers plan to tell participants afterwards. The researcher(s) confirmed that this is discussed with participants as part of the standard process.
7. The committee queried whether participants will be asked to complete a food diary at beginning of the study before consenting. The researchers confirmed that they are hoping to ask people to do this (the have the food diary available at the first visit). The committee noted that the food diary is a study procedure; study procedures cannot commence before consent. The committee asked that participants are invited to consent to this before taking part in any study procedures.
8. The committee noted that the researchers will collect information about income at screening and asked whether there is a reason for this. The researchers explained that this is a standard measure that they use and they have collected this information is almost all studies they have done.
9. Please advise in the PIS that you will provide a copy of blood tests back to participants’ GPs.

Decision

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

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

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

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| **6** | **Ethics ref:** | **16/NTA/40** |
|  | Title: | Automated assessment of functional recovery by an assistive device. |
|  | Principal Investigator: | Mr Michael Sampson |
|  | Sponsor: | Callaghan Innovation |
|  | Clock Start Date: | 31 March 2016 |

No member of the research team was present for discussion of this application.

Potential conflicts of interest

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

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

Summary of ethical issues

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

1. The committee was uncertain on a number of questions such as, how they are recruiting participants, how the 4 groups of participants are different. Conflicting information about inclusion of fit volunteers vs patients with stroke or brain injury were noted. The researchers have not provided a rationale in the application about why this study is being done, the protocol provided was minimal, there is no information about the study design, no controls, and no detailed information about what the researchers intend to measure. Although it was stated that only measurements were being taken, the text indicates the device is for therapeutic purposes and the measurements were additional, how these are related is unclear. It is also not clear to the committee who will collect participant data and also what data is being collected. The committee agreed that it did not have enough information in this application to make a decision. In addition, the Participant Information Sheet does not contain any information on study procedures at all.
2. Inclusion and exclusion criteria- it was not clear to the committee about whether the participants will have functional capacity to consent. The researchers have given no indication that they consider that the possibility of participants not being able to consent is an issue and indicate that is appropriate for the family to consent which it isn’t as in New Zealand, participants themselves must consent to taking part in research.
3. The committee noted that the changes/queries stated in the scientific peer review document provided with this application appear not to have been addressed. The researchers appear not to have addressed issues noted particularly around consent and approach of patients. The committee agreed with the queries raised in the peer review document and was not satisfied that they have been satisfactorily addressed in the application submitted for review.
4. The committee would like to see what individualised feedback to participants will look like and how the researchers are going to do this.
5. The committee noted that the researchers state that consultation with Mãori was carried out for a previous trial but there was no mention about what was covered as part of this process. The answers stated at questions p.4.1. and p.4.2 on the application form were not adequately answered.
6. p.4.1. Please describe whether and how your study may benefit Māori. The answer should include incidence and prevalence (statistics) of the disorder under study (or treatment indication if a drug trial) in Maori. The Secretariat notes that some disorders are particularly important for Maori health, while others are relatively rare in Maori and may have less of an impact. If the impact of treatment or prevalence of disease is low or the same as other populations please state this clearly to the Committee. Generally, any available statistics relating to Maori should be provided where possible.   
     
   If the study is an early phase trial, a caveat that no benefit is expected as a direct result of the study.   
   If relevant, please include information on how researchers will ensure that Maori benefit at least equally (and actually how they can disproportionately benefit if they are disproportionately represented) –for example, what extra measures if any are in place to ensure Maori participation (iwi consultation, Maori researchers, active follow up etc) as well as interpretation of results and presentation of findings back to those consulted. The Secretariat notes this could be explained in the question about consultation.

### p.4.2. Please identify the main cultural issues that may arise for Māori who may participate in your study, and explain how these issues will be managed.

The Secretariat notes that the study contains potential cultural issues. While these issues will be raised in consultation, which can occur after HDEC review, the Secretariat notes that the application has not been correctly completed and requests that researchers seek guidance in completing their application in future.

p.4.3.1. Please either describe your study’s consultation process, or explain why you do not consider that formal consultation with Māori is required.   
The Secretariat notes that while evidence of consultation does not need to be submitted prior to HDEC review, the Committee does need to know the planned consultation process for the main sites. Please explain the consultation process i.e. who; what; where; when and how. Please include names or institutions of those you will consult with. The Secretariat noted that there is guidance on the level of consultation required from the HRC Guidelines for Research Involving Maori and Te Ara Tika. Please refer to these documents if possible.

The committee noted that application 15/STH/144 mentioned in the application form related to a previously built device. The committee would like to see this application included in any future application.

Decision

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

5.2 Investigators should develop clear study questions that identify the participant population,

the intervention and the main outcome of interest. Normally the outcome(s) to be studied should be clinically significant.

5.11 Peer review of the scientific validity of a study’s protocols is beneficial and is advised for all studies that pose more than minimal risk.

Services may be provided to a consumer only if that consumer makes an informed choice and gives informed consent, except where any enactment, or the common law, or any other provision of this Code provides otherwise. *(Health and Disability Commissioner Code of Rights, Right 7(1), Right to make an informed choice and give informed consent)*

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| **7** | **Ethics ref:** | **16/NTA/42** |
|  | Title: | A study assessing the similarity of Avastin® and the trial drug CBT 124 |
|  | Principal Investigator: | Dr Christian Schwabe |
|  | Sponsor: | Quintiles Pty Ltd |
|  | Clock Start Date: | 31 March 2016 |

Ms Hannah Palmer and Dr Leanne Barnett were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of the study

1. The committee asked the researchers to outline the study briefly and to comment in particular on why they are doing a first-in-human study in New Zealand for this type of medication and why they have a large sample size for this first-in-human study.
2. The researchers stated that this is a bioequivalence study, which aims to show that CBT 124 has a high degree of similarity to Avastin® to aim for cheaper treatments for this type of medication.
3. A total of 150 male volunteers in New Zealand and Australia (75 in New Zealand). The committee queried why such large numbers to assess bioequivalence. The researchers explained that the study design is a 1:1:1 ratio with study drug vs two branded drugs (EU and US), which means a large sample size. The researchers noted that the sample size in this study is similar to other phase I studies they have done. The committee suggested that this number still seems large for a first-in-human study and requested that the researcher(s) provide comment on this, and why it is required to assess against both EU and US preparations.
4. The researchers advised that they recently finished dosing for similar study with 3 groups in a 1:1:1 ratio with the EU approved Avastin® vs US approved Avastin® bio equivalent for a sponsor done in India. That study was approved by the Southern HDEC committee and recruited 150 subjects for a first-in-human monoclonal antibody. The committee were interested to see the ethical review of this study and asked that the reference number be provided.

Summary of the ethical issues discussed:

1. The committee queried whether the research team have a bio statistical rationale for the sample size in this study as it did not see it as part of the protocol or IB submitted with this study. The committee would like to see a justification of the sample size from the sponsor.
2. The committee asked whether Avastin® is still on patent and the researchers advised that it will shortly come off patent and these trials are in preparation for this.
3. The committee checked its understanding that participants will be randomised to receive a single lowest dose of the drug and will stay on site for 3 days. Treatment will be randomly allocated in a 1:1:1 ratio. The first cohort will include 3 participants, the second 6 participants and the third 9 participants then 150 total and 14 weeks of follow up. 11 visits over 14 weeks. The committee queried what the researchers experience safety of participants was in the other bio similar trials. The researchers explained that in a recent study they had medical staff on site for 24 hours following dosing and no acute reactions were observed. The researchers commented on a similar bioequivalence study for another sponsor where there was 2 weeks of inpatient monitoring. There were no serious adverse events,the adverse events were not attributed to the study drug. The researchers noted that common side effects included headache, lower back pain and a couple with minor injuries in follow up period. The researchers confirmed that in the IB there are no SAES for Avastin® in with healthy adults with a single dose and this is still their understanding. The committee queried why there was such a large discrepancy between 2 weeks in the previous similar study and 3 days in patient monitoring. The researcher(s) stated that they believed 2 weeks was unnecessarily precautionary, and that they were comfortable with the safety of the 3 day inpatient stay in this protocol.
4. The committee queried how the researchers intend to recruit participants to the study noting that the application mentions a website. The researchers explained that they have a database that they use to inform people of new studies and that if interested they can get in touch via email or telephone for more information and to confirm whether they would be interested in participating. The research team may also use radio and or print advertising. The committee queried whether ACS has any rules/policy in place around how often people can participate in trials. The researchers advised that they do and that participants cannot enrol in further trials if they have been in another trial in the last three months.
5. The committee queried how the pay compared in the previously approved HDEC application. The researchers explained that in that study there was a significant inpatient stay compared with this study which is for three nights. The length of stay is a sponsor decision and in the previous study they wished to monitor participants for longer following dosing. There are no safety concerns in this study and the sponsor considers three days to be long enough based on the results of the previous study. It was not clear to the committee whether the risks had changed in this study and the committee queried whether the pay offered in this study is proportional to the risks these participants will face. The committee would like reassurance on these aspects.
6. The committee noted that the researchers have stated that any serious adverse events will be monitored by an internal data safety monitoring committee and asked who will make up this committee. The researchers advised that committee will be made up of the principal investigator in communication with the study sponsor.
7. The committee queried how long the researchers intend to observe the first cohort before they give the dose to the second cohort (staggered administration; within group randomisation for n=3, 6 then 9 before the remainder of participants are randomised). The researchers advised, as the protocol specifies, that participants will be discharged 48 hours post dose on Day 3. The committee requested that the research team submit a progress report after the third stage and before they go on to complete dosing the remaining participants.
8. The committee noted that the drug is being developed in India and queried whether the drug is being developed for the Indian market. The committee queried why it is being tested here in New Zealand and whether there will be any benefit for New Zealanders?

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

1. Page 8, ‘Testing and Storage of Samples’: it is mentioned that participants tissue samples will be destroyed 1 month after the study has completed. The same statement is included in the consent form. However, it is clear in other parts of the application that the samples will be stored for 10 years. The researchers noted that this is likely in error and will follow up and confirm.
2. Page 9, ‘What are the risks of Avastin®/CBT124?’: please include quantification of the risks. For example, more than 10 percent have experienced X. The committee noted that Epistaxis is mentioned in the IB and asked that it be included here in lay language.
3. Please include the name and contact details for the Mãori support person for this study.
4. The committee commented for ACS that HIV stated as being notifiable when it is not. Aids is notifiable but HIV isn’t. If participants are diagnosed with HIV then they would be advised to talk to their GP and get appropriate counsel.

Decision

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

* Please amend the information sheets and consent forms, taking into account the suggestions made by the committee *(Ethical Guidelines for Intervention Studies, para 6.22)*
* Justification as to why drug is being tested here in New Zealand and whether there will be any benefit for New Zealanders.
* Whether the pay offered in this study is proportional to the risks these participants will face. It was not clear to the committee whether the risks have changed in this study. The committee would like reassurance on these aspects.

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

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| **8** | **Ethics ref:** | **16/NTA/44** |
|  | Title: | Study on the effect of Lambda in patients with Chronic Hepatitis D Infection |
|  | Principal Investigator: | Professor Edward John Gane |
|  | Sponsor: | Pharmaceutical Solutions |
|  | Clock Start Date: | 31 March 2016 |

Ms Amy Cole was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of the study

1. There is currently no approved therapy for CHD. Current therapy suppresses Hep B infection but not Hep D, which is an aggressive virulent virus and takes effect on the liver. Participants who are taking medication to treat Hep B will continue to take that medication.
2. The committee asked how different the drug to be tested is from alpha. It is a different structure and has fewer side effects.
3. This multi-centre study will aim to recruit 5 patients in New Zealand. Hep D is rare and occurs most commonly in eastern European and Samoan peoples. The researchers will not actively recruit Samoan people. Mãori consultation is with Helen Wihongi.

Summary of ethical issues discussed:

1. Administration of subcutaneous injection? Self-injecting patients are used to doing this if they have Hep B. For some this might be a new process but regardless, the research team have methods in place to help make the procedure as accessible as possible. The researcher(s) will provide small needles and a sharps disposal container for needles for participants to use in the community as is standard practice.
2. The committee noted that the answer stated at question p.4.2 on page 26 of the application form did not answer the question. The committee noted that genomic testing of samples is one issue that could have been identified in this question as being relevant to Maori. The researchers advised the cultural issues for Maori will be addressed as part ADHB Maori consultation process.
3. The committee stated generally speaking in regard to the use of samples for future unspecified research and pharmaco genomic research that it would like to see researchers push back on the sponsors when they say that there are no risks involved. The committee emphasised that there are informational and privacy risks involved.

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

1. Please include more detailed information about the subcutaneous injection including that the first dose will be administered by clinic staff in the clinic on day 1 and that clinical staff will then provide training and information on the sub-cutaneous injection on day 1.
2. Please review the documents for typos and grammar. The committee noted in particular, pages 3, 7 and 11.
3. Page 9, ‘What are the benefits of being in this study?’: the committee thought that the benefits included here were overstated and also queried whether they were cut and copied in. Please review this information and change it if needed.
4. Page 10: the committee noted that the compensation statement included in this section is outdated, is litigious and implies protection of the company rather than the individual. Please replace the statement with the following from the HDEC pro-forma: “Commercially sponsored” intervention studies: *If you were injured as a result of treatment given as part of this study, which is unlikely, you won’t be eligible for compensation from ACC. However, compensation would be available from the study’s sponsor, [x], in line with industry guidelines. We can give you a copy of these guidelines if you wish. You would be able to take action through the courts if you disagreed with the amount of compensation provided. 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.*
5. Pages 11 and 12, ‘Is participation in this study voluntary?’: some of the reasons given for the company withdrawing participants from the study are not allowed in New Zealand. Pleasereview and remove the following statements: “There are problems regarding financing of the research or with the supply of the study preparation.” “There is another reason that the sponsor considers to be important.”
6. Please clarify the following statement: “There are problems regarding fulfilment of the study requirements.”
7. Page 11, ‘Handling of Samples’: the committee noted the statement that should Mãori participants have any concerns regarding the appropriate practice/tikanga to address cultural issues arising from their participation in the study that it is recommended that they “consult someone they trust”. The committee suggested that they could also include reference to someone within the research team and include the details of a Mãori contact person on the last page of the document.
8. Optional research information sheet: ‘Who pays for the optional part of the study?’ please review and remove this statement.
9. Optional research consent form: Please include the statement about samples being sent overseas so that you can check and show that people understand and consent to this.
10. Consent forms: please remove the words “Description of Legal Representative’s Authority (e.g., parent, guardian, etc.)”

Decision

This application was *approved* by consensus.

Non-standard conditions.

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

## Substantial amendments

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| **1** | **Ethics ref:** | **15/NTA/146/AM01** |
|  | Title: | The ABC Study: Assisted breathing before cord clamping |
|  | Principal Investigator: | Mrs Elizabeth Nevill |
|  | Sponsor: | Dr Shamshad Karatela |
|  | Clock Start Date: | 29 March 2016 |

Mrs Elizabeth Nevill and Mr Mike Meyer were present in person for discussion of this amendment.

Potential conflicts of interest

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

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

Summary of ethical issues

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

1. The committee established that the amendment is seeking approval for non-consensual research; where the intervention has already been performed and that the researchers are seeking parental deferred consent to collect and use the outcome data in this study. The researcher(s) confirmed that they intend to seek prospective consent as far as possible and intend delayed consent to be restricted to those patients who present to hospital in established labour and are therefore potentially not able to provide fully informed consent at this time. The researchers confirmed that the will not collect or use the outcome data if parents do not give their consent.
2. The researchers further added that they are dealing in emergency situations cannot always feasibly get consent to collect and use the data when a woman is in active premature labour.
3. The researchers have consulted widely and have included the Patient Whanau Centred Care consumer council meeting minutes, which set out their discussion and community consultation, communications with the anaesthetic team, the assessment midwifery team, the Maaori Research Review Committee and the CMH legal team letter of response.
4. The committee noted that the evidence of communications with the above groups showed that they supported the proposal for deferred consent to collect the outcome data, including highly supportive comments from parents of premature babies (the target audience).
5. The legal opinion submitted with the documents argued that enrolment in the study is in each participant’s best interests as they will be subject to “inclusion benefit”- better monitoring and care associated with being in research.
6. In the current study, the potential risks are low while the benefits of assisted ventilation may prove to have significant clinical advantages for very preterm infants. A German study which included this intervention as part of a package of care in a group of babies born before 26 weeks gestation showed improved outcomes in terms of Intraventricular Haemorrhage (IVH). Outcome changes were noted in these infants in a pre and post comparison for this package of care, which was suggestive of improved outcomes. Package of care elements tested overseas in these studies did not suggest any negative outcomes. Even small improvements for these infants are important in terms of long term development and function.
7. Right 7(4) legal opinion: the committee noted that the legal report had noted “inclusion benefit”. For the committee to approve the gaining of delayed consent it would need to be satisfied that participation would be in the best interests of each participant.
8. The committee and the researchers discussed the point of best interest for the infants and parents. As noted previously overseas evidence is supportive of better outcomes with a package of care that included this intervention. The procedure is safe and is already current recommended practice, the intervention simply brings the resuscitation time point forward; earlier than is current practice. In the trial half will get standard care and other half will have standard resuscitation practice and will do the intervention a little earlier than usual. All babies will receive this as standard of care and some will receive it sooner and get more care. That babies will do better if they have interventions on basis that breathing stabilisation is well recognised as clinically important.
9. The committee asked the researchers to show whether they believed that performing the procedure a little earlier than happens in standard of care would be in the best interests of each participant. The researchers said that they were doing this work in their own time and that they wouldn’t go to such lengths if they didn’t believe that it would be beneficial. This work is a logical progression of the improvements in neonatal care, and they have identified a vulnerable group and this is the next step to getting better outcomes for these babies. The research forms part of a series of incremental steps.
10. The researchers noted that other studies had been approved with deferred consent. In these studies the researchers described immediate benefits as well as they are getting more care in ICU. There is a direct outflow effect on parents and family so a whole group of potential benefits. The committee accepted that there may be an immediate benefit to participants if IVH is prevented such as less time in ICU, and that having earlier parental ability to hold baby is an important additional benefit.
11. The researchers intend to measure outcomes on both short and long term basis. In the short term they will look at outcomes on the basis of echo cardiogram, resuscitation outcomes and in the long term on all other neo natal outcomes. The longer term follow up is important and they intend to do this to two years as is standard of care.
12. The committee asked whether, if the outcome data showed earlier intervention ie earlier giving of oxygen does make a significant difference that they could implement this as the gold standard of care earlier than the two years. The researchers confirmed that this could be possible. The researchers noted that centres overseas are routinely using this as standard of care.
13. In terms of the issue about only including prospectively consented participants, the researchers noted that this would skew the results of this study as the data captured would be only from the population that attended antenatal care and would exclude the group of women who have not accessed antenatal care and are most at risk of infants with poor outcomes. They have demonstrated this in their previous studies, and provided the literature with their last application.
14. The researchers have to date consulted with 12 women in antenatal care and 3 of those women were enrolled into trial with prospective consent. The researchers had no declines to enter the study but not all of the 12 women went on to have premature births.
15. The committee voted on whether it was satisfied that participation in this study would be in the best interests of each participant and therefore whether it would approve deferred consent from parents to collect and use the outcome data.

Decision

This amendment was *approved* by vote, with 7 for and 1 against, and Dr Christine Crooks dissenting.

## General business

1. The Committee noted the content of the “noting section” of the agenda.
2. The committee would like to know more about how Medsafe/SCOTT scientific review process works and what is checked.
3. The Chair reminded the Committee of the date and time of its next scheduled meeting, namely:

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| **Meeting date:** | 10 May 2016, 01:00 PM |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

The following members tendered apologies for this meeting.

* Dr Charis Brown

The meeting closed at 5:20pm.