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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 13 September 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 9 August 2016. |
| 1.30pm | New applications (see over for details) |
|  | i 16/NTA/131  ii 16/NTA/149  iii 16/NTA/132  iv 16/NTA/133  v 16/NTA/134  vi 16/NTA/139  vii 16/NTA/140  viii 16/NTA/141  ix 16/NTA/142  x 16/NTA/144  xi 16/NTA/146  xii 16/NTA/148 |
| 6.00pm | General business:   * Noting section of agenda |
| 6.20pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Brian Fergus | Lay (consumer/community perspectives) | 11/11/2015 | 11/11/2018 | Present |
| Ms Susan Buckland | Lay (consumer/community perspectives) | 11/11/2015 | 11/11/2016 | Apologies |
| Dr Karen Bartholomew | Non-lay (intervention studies) | 13/05/2016 | 13/05/2019 | Present |
| Dr Christine Crooks | Non-lay (intervention studies) | 11/11/2015 | 11/11/2018 | Apologies |
| Ms Shamim Chagani | Non-lay (health/disability service provision) | 11/11/2015 | 11/11/2016 | Apologies |
| Dr Kate Parker | Non-lay (observational studies) | 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 |
| Mrs Phyllis Huitema | Lay (consumer/community perspectives) | Co opt NTB | Co opt NTB | Present |
| Mrs Leesa Russell | Non-lay (observational studies) | Co opt NTB | Co opt NTB | Present |

## Welcome

The Chair opened the meeting at 12.48pm and welcomed Committee members, noting that apologies had been received from Mrs Shamim Chagani, Mrs Susan Buckland and Dr Christine Crooks.

The Chair noted that fewer than five appointed members of the Committee were present, and that it would be necessary to co-opt members of other HDECs in accordance with the SOPs. Mrs Leesa Russel and Mrs Phyllis Hutiema confirmed their eligibility, and were co-opted by the Chair as members of the Committee for the duration of the meeting.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

## Confirmation of previous minutes

The minutes of the meeting of 9 August 2016 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **16/NTA/131** |
|  | Title: | Riociguat rEplacing PDE-5i therapy evaLuated Against Continued PDE-5i thErapy |
|  | Principal Investigator: | Prof Lutz Beckert |
|  | Sponsor: | Bayer New Zealand Limited |
|  | Clock Start Date: | 01 September 2016 |

Mrs Liz Cousins was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This clinical research study will test a new approach for the treatment of patients with pulmonary arterial hypertension (PAH). The purpose of this study is to demonstrate the effectiveness of Riociguat as replacement of PDE-5i therapy (Sildenafil or Tadalafil) in patients with pulmonary arterial hypertension (PAH) who are on a stable dose of phosphodiesterase-5 inhibitors (PDE-5i: Sildenafil or Tadalafil) with or without endothelin receptor antagonist (a drug that blocks endothelin receptors), but the treatment has not reached its goal.
2. Riociguat, as monotherapy or in combination with endothelin receptor antagonists, is indicated for the treatment of adult patients with pulmonary arterial hypertension (PAH) to improve exercise capacity.
3. This study will involve up to 9 study visits and 2 telephone contacts over a period of 30 weeks.
4. Patients, who qualify for this study, will be randomised to get one of the following treatments:

• Treatment 1: Riociguat – the participant starts with a dose of 1mg, three times a day. For the first 8 weeks of the study, the study doctor will adjust the Riociguat dose for up to 2.5mg, three times a day. There may be a dose adjustment during the study, according to the participant’s health status and symptoms.

• Treatment 2: the participant continues his/her current PAH treatment with Tadalafil or Sildenafil as well as other supportive treatments at the discretion of the study doctor.

1. During the study, according to the participant’s symptoms and the study doctor evaluation, another PAH specific drug can be given.

Summary of ethical issues (resolved)

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

1. The Committee noted that this study did not involve bio-banking.
2. The Researcher(s) confirmed interpreters were provided if needed.
3. The Researcher(s) explained that both New Zealand sites would not participate in the MRI sub-study. The Committee stated they would not consider or approve that sub-study in this approval, but if another site wanted to opt in, they could submit an amendment.
4. The Researcher(s) confirmed identifiable data is not sent to the Sponsor. The Researcher(s) explained that monitors would access the data for quality purposes.
5. The Committee queried if there is any washout risk (24 hours). The Researcher(s) stated there is no risk.

Summary of ethical issues (outstanding)

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

1. R.1.6 – remove any mention of terminating a study for commercial reasons from the participant information or other study documentation. New Zealand ethical guidance states studies should not be terminated simply for reasons of commercial interest or public relations.
2. R.3.7 – please make sending samples overseas very clear, including where they are going and that New Zealand will not have oversight for future use.
3. The Committee queried whether visits are at home (2, 4 and 6) or are they at the clinic. The Researcher(s) stated the location for visits are flexible, they could be in clinic or at home depending on the location of the participant. The Committee requested this is clearly explained to participants, and clarify whether it is the participant’s choice or the sites choice.
4. The Committee asked for clarification around the timing of sending the GP letter, noting it was sent before participants were actually confirmed to be enrolled. The Researcher(s) stated once the participants are consented, the final inclusion exclusion criteria are based on the baseline tests, so while they are ‘in the trial’, they may not end up eligible to take the study drug. The Committee queried whether GPs could be informed when the participants are actually in the trial, including meeting baseline requirements. The Researcher(s) confirmed this was possible. The Committee stated this process should be followed. Please take that back to the Sponsor and confirm it is acceptable.
5. The Committee queried page 18 of the PIS on data use; ‘I understand and agree that my data, medical records etc’. Is this statement referring to de-identified data? Who will access the data? This is currently problematic as it is a very broad statement. The Committee also noted that this information should be removed from the consent form and placed in the Participant Information Sheet.
6. The Committee asked whether participants who have withdrawn would continue to have data collected about them. The Committee requested that if someone withdraws no *further* data is collected. The Researcher(s) stated they would clarify with the Sponsors.
7. The Committee queried how long participants were followed up – please let HDEC know via cover letter and include details in Participant Information Sheet.
8. The Committee noted that 16 of 22 of the Participant Information Sheet contains some language that implies future unspecified research. Please explain in full. If the Sponsor confirms that the study involves future unspecified research please email HDEC to ensure all requirements are met prior to response of the HDEC decision.
9. The Committee queried whether the study drug was available after the study (post trial access). The Researcher(s) noted that a prior study had an extension study available, but for this study, because it is not an approved medication, it is not clear whether the Sponsor will offer an open label extension. The Committee stated they wanted the researcher to check with the Sponsor and justify either proving access or not, and if not – make it very clear to participants in the Participant Information Sheet.

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

1. The Committee queried why information on the termination of a related study is not added in the Participant Information Sheet. The Researcher(s) explained that the terminated study is still being investigated, but it related to treating a different condition, but the information about the drug being used for its intended indication are still valid. The Committee requested that this information is added in lay language, making it clear that it was being used for a different condition.
2. Revise for clinical jargon. Explain in lay language.
3. Make it clear what phase the trial is, and what this means for participants.
4. Please use the HDEC template; current layout is plain and hard to read. Readability, in terms of white space and logic of sections, can be improved.
5. Insurance company is mentioned as if everyone will have insurance, this is likely due to the document being developed in America. Please reword, ‘if’ you have insurance, and ‘may’ cover.
6. Please remove legal representative section on consent form.
7. Please remove witnesses, not required.
8. The Committee noted the consent form reads from a very legal point of view, please revise with regards to the HDEC template.
9. The Committee noted consent form contains information that is not in the Participant Information Sheet. Any information should be in the Participant Information Sheet rather than the consent form. Please track changes.
10. Make it clear that drug screening will occur, as drug users are excluded from this study. Blood testing for such purposes should be clearly explained to participants.

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Provide further information on the study design, in a cover letter that addresses outstanding ethical issues listed (*Ethical Guidelines for Intervention Studies para* 5.4)

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

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| **2** | **Ethics ref:** | **16/NTA/149** |
|  | Title: | A study of the Relative Oral Bioavailability of AL-3778 Capsules and Tablets and Drug Interaction in healthy subjects |
|  | Principal Investigator: | Dr Christian Schwabe |
|  | Sponsor: | Alios BioPharma, Inc |
|  | Clock Start Date: | 01 September 2016 |

Dr Christian Schwabe and Mrs Hannah Palmer were present in 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 three-part study. Up to 114 healthy adult male and female subjects, 18 – 60 years of age will be enrolled into this study. Eighteen subjects will be enrolled in Part 1 (and in Part 2 if conducted). Up to 78 subjects will be enrolled in Part 3.
2. Part 1: This part is to evaluate the relative oral bioavailability of the study drug (AL-3778) when given as a capsule under fasted conditions and tablet under fasted and fed conditions.
3. Part 2: this is the optional component that may be conducted at the discretion of the Sponsor in consultation with the PI based on the results from Part 1. Part 2 will be conducted in the event bioavailability of the 600 mg dose of tablet is lower than expected and may explore other tablet dosages.
4. Part 3: is being conducted to evaluate the potential drug interactions between the study drug and two other anti viral Hepatitis B medications; entecavir and tenofovir disoproxil fumarate.

Summary of ethical issues (resolved)

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

1. The Committee queried why there are so many parts to this study. The Researcher(s) explained this is a compound they have tested in first in human study a few years ago. There is a flurry of development activity to find a functional cure for hepatitis B. This cure is likely to be a combination therapy that targets multiple life cycles of the virus.
2. The Researcher(s) explained in the first study they used a suboptimal formulation of this study drug. The Sponsor would like to improve that formulation, and test a tablet rather than a capsule formulation. The Sponsor is not sure whether the tablet will deliver what they expect, which is why the part 2 is optional. The first part compares old delivery method vs. the tablet. The higher dose will occur if the bioavailability is less than expected, in phase 1.
3. The third part of the study is a drug-drug interaction component. This is important information in order to develop the drug to be feasible for patients with chronic hepatitis B.
4. The Researcher(s) explained first in human was in 2014. It has been two years since they first saw this compound. There is a fair amount of safety information on the drug, from volunteers and patients. The Researcher(s) acknowledged the compact design, and noted the study aimed to answer two questions (drug interaction and bioavailability).
5. The Researcher(s) confirmed first in human was single dose and multiple ascending doses. This also had 14 and 28 days.
6. The Committee queried what the data safety monitoring was in the first in human study. The Researcher(s) noted the first in human was uneventful, with patients there was one serious adverse event that is fully outlined in the protocol.
7. The overall safety profile of this compound has nothing of particular to note. The Committee noted the extensive information in the protocol about the drug. The Researcher(s) noted the preclinical information that supported entry into human study.
8. The Committee queried the recruitment. The Researcher(s) explained they have 6500 previous participants who participate in healthy volunteers. The Researcher(s) will contact them first, though if that method is not sufficient, we will then advertise - usually by radio.

Summary of ethical issues (outstanding)

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

1. R.1.4 states no formal data safety monitoring. Please explain. The Researcher(s) stated we initially stated internal data safety monitoring, which in reality is what we are conducting. The Sponsor had changed it during the application. The Researcher(s) confirmed it was a formal, internal, data safety monitoring.
2. The Committee queried the Researcher(s) views on the umbrella protocol method. The Researcher(s) explained they often use this trial method, where trials change based on phases of each study. The Researcher(s) noted the prior study was approved using this method, and that this study is further down the track. The Committee requested an update at each step for each of the 3 steps, and any resulting amendments. The Committee stated a progress report or an amendment were appropriate.

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

1. The randomisation and timing of treatments, particularly of part 3, is confusing. Please consider a table or diagram.
2. The Committee noted the pregnant partner Participant Information Sheet is unchanged from the American context. Please review for a New Zealand context.
3. The Committee queried where the PK studies were conducted. The Researcher(s) stated California. Add to Participant Information Sheet.

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Provide further information on the study design, *outlined in the outstanding ethical issues* (*Ethical Guidelines for Intervention Studies para* 5.4)

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

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| **3** | **Ethics ref:** | **16/NTA/132** |
|  | Title: | Acerta 309 |
|  | Principal Investigator: | Dr Peter Ganly |
|  | Sponsor: | Pharmaceutical Research Associates Ltd NZ |
|  | Clock Start Date: | 01 September 2016 |

Dr Peter Ganly was not present for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This is a study in CLL patients who have had a return of disease despite treatment. This study is designed to evaluate the effectiveness of the new drug acalabrutinib alone compared with the two currently available drug combinations idelalisib/rituximab or bendamustine/rituximab.
2. The effectiveness is determined by measuring progression free survival that is to be confirmed by an independent review committee.
3. It is designed such that participants will remain on the study for so long as the drug remains effective, with the possibility to cross onto the study drug arm if the combination drug arms fail.

Summary of ethical issues (outstanding)

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

1. The Committee queried why there are not follow up pregnancy tests, noting the risks to unborn child.
2. The Committee queried what ‘poor enrolment’ means in terms of terminating a study. Please explain whether enrolment has been thought about to ensure the study is not terminated for commercial reasons.
3. The Committee queried what ‘access to best medicine’ means in this context. Please explain to HDEC and for the participant in the Participant Information Sheet. For instance, can participants stay on experimental treatment after the study?
4. Please explain data safety monitoring committee arrangements. Is there international, as well as internal?
5. The Committee requested confirmation that the Sponsor will never access identifiable information (page 24 Participant Information Sheet).

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

1. Review for language of liver enzyme elevation for a lay participant. Explain what the practical implications of raised liver enzymes
2. Please explain to a layperson what the table of radiation mean. The Committee queried whether it is correct that there is actually no increased radiation.
3. Remove yes/no tick boxes unless the statement is truly optional. (consent form).
4. Pregnancy data – keep data 10 years after child turn 16.
5. R.1.1 – talks about risk of study but not risk of being on experimental drug.
6. Please consider using a table.
7. Revise the bold use throughout the Participant Information Sheet.
8. The Committee noted the Participant Information Sheet is over ten thousand words. Please revisit repetition, and try to reduce.
9. Page 10 – states Sponsor will use blood and tissue samples, taken during the study. The Committee queried whether results could be returned? Are these samples de-identified?
10. Review for typos.
11. The Committee queried the lack of a Māori tissue statement in the Participant Information Sheet. The committee recommended the following statement: *You may hold beliefs about a sacred and shared value of all or any tissue samples removed. The cultural issues associated with sending your samples overseas and/or storing your tissue should be discussed with your family/whanau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult prior to participation in research where this occurs. However, it is acknowledged that individuals have the right to choose.”*
12. Make it clear that alternative medical options are offered while talking about the study, not after declining to participate.

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Provide details of the Data Safety Monitoring Committee’s composition and monitoring plan *(Ethical Guidelines for Intervention Studies para 6.50).*
* Please provide criteria for study termination. (*Ethical Guidelines for Intervention Studies* *para 6.64*).
* Inform the Committee of the outcome of the request for post-trial access. Please also provide information on what participants are told. (*Ethical Guidelines for Intervention Studies* *para 6.67*).

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

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| **4** | **Ethics ref:** | **16/NTA/133** |
|  | Title: | Whare Aroha transition study |
|  | Principal Investigator: | Associate Professor Stephen Neville |
|  | Sponsor: |  |
|  | Clock Start Date: | 01 September 2016 |

Mrs Kay Shannon 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. Rotorua Continuing Care Trust operate an aged residential care facility, Whare Aroha Care, providing rest home, private hospital and secure dementia care. The trust is building a village, primarily but not exclusively for people with dementia.
2. Based on the Hogeweyk model, people will live in domestic scale environments with like-minded others. The research will explain the resettlement of Whare Aroha Care residents into the village and the effects of the resettlement on the lives of the residents.
3. The study will utilise a critical realist methodology and a single case study research design. The initial theoretical propositions for the study will draw on the Hogeweyk care concept. Study participants will be facility management, staff, residents and family members as well as other key informants from organisations such as the Ministry of Health.
4. Study data will be collected using interviews, focused observation and document examination, guided by the theoretical propositions for the study. Iterative data analysis will occur parallel to data collection, guided by the theories identified at the beginning of the study and refined during the course of the study. Beginning with coding and progressing to abstraction, analysis will build explanations of the transition to the new village and the effects of the transition on resident lifestyle.
5. The village will be the first based on the Hogeweyk model completed outside the Netherlands, with the setting adapted to the New Zealand lifestyle, including a cultural house for people accustomed to living a Māori cultural way. The study is unique because it seeks to provide robust qualitative evidence about the transition to a dementia-friendly village and its’ effects on the lives of residents. The results of the study will be useful to policy makers and to other organisations seeking to develop villages based on the Hogeweyk model and adapted to their local contexts.
6. Current care is private level care, hospital care and secure dementia care. The new model of care places patients with others who have had a similar life rather than those of a similar level of dementia. For example, houses that look like estate houses, forestry houses or other industry houses. There are also remote houses or cultural houses. The idea is that you live in a way and setting that makes the patients comfortable.

Summary of ethical issues (outstanding)

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

1. The Committee asked for clarification about the three methods of observation: interviews, photos and general observations. The Researcher(s) explained what would occur, adding there is also an analysis of documents.
2. The Committee noted the submission did not have any questionnaires submitted, for either of the participant groups (patients, families etc.). The Researcher(s) explained two interviews will be offered to the patients (residents). One is a formal interview, the other is following them during an activity (informal). Questions will range from ‘how does it feel living here’, ‘what are you able to do here’ etc. The Researcher(s) explained that because it is a village there could be chance encounters. The Committee requested all documentation relating to questionnaires and interviews, even if unstructured.
3. The Committee noted there needs to be consideration around when this interview takes place, and ensure the discretion of the participant is considered. Please provide information on ensuring potential risks involved in interviews are managed.

Consent in this population:

1. The Researcher(s) explained that staff has access to a range of cognitive function tests (which are standard in this context). The Researcher(s) explained the staff would identify the residents who are identified as able to participate on their own.
2. The Committee noted there would be a range at the further end of the spectrum who could not consent. The Researcher(s) confirmed they expected that some would not be able to provide their own consent. The Researcher(s) explained the family member who makes their decisions for them usually, would be approached to state that participation would be in the patient’s best interest.
3. The Committee explained that the application includes the provision for proxy consent for participants unable to provide their own informed consent. However, in New Zealand, proxy consent for research is only legally acceptable in cases where the medical experiment would save the person’s life or prevent serious damage to the person’s health. Therefore, the form for the participant’s representative should only be used to gauge views of relatives/ friends/ EPOA of potential participants involved that are unable to consent for themselves. This means that the forms should not involve language whereby the relative/friend/EPOA consent on behalf of someone else. As an alternative, the language should reflect that the document seeks the friend/relative/EPOA’s view that the non-consenting person would be agreeable in participating. This is in line with Right 7(4)cii of the HDC Code of Rights: If the consumer's views have not been ascertained, the provider takes into account the views of other suitable persons who are interested in the welfare of the consumer and available to advise the provider.
4. The Committee stated that it is not possible for HDECs to approve an application unless it is consistent with New Zealand law. Research involving participants who are not competent to consent is inconsistent with New Zealand law, unless undertaken in accordance with Right 7 (4) of the of the Code of Health and Disability Services Consumers’ Rights. In addition to requirements regarding ascertaining the views of the consumer and other suitable persons (forms consistent with this aspect are currently included in this application), Right 7(4) of the Code requires that any health services provided without the informed consent of the consumer must be in the best interests of the consumer. This means that there must be some benefit, or potential benefit, to the participant beyond what they would receive if they were not participating in the research.
5. The Committee explained the potential benefits for those individuals, for example giving individuals opportunity to reflect and change their direct environment. This opportunity held a benefit as they would be able to raise any issues they had directly, and have support in the transition from one environment to the other.
6. The Committee noted the need to have a cover letter explain in detail:

- the level of competency levels and the corresponding consent and methods used to enrol them.

- Importantly it will need to be clear why it would be in someone’s best interests to participate.

- the letter should reflect the requirements set out in the Code of Rights.

1. The Researcher(s) explained what information they can add to the Participant Information Sheet to know more about what the study is actually about. The Committee agreed that more information was needed
2. The researcher explained the protocols to determine if someone lost capacity to consent, or whether they were displaying dissent.
3. The Committee noted the photos were not well explained in the Participant Information Sheet.
4. The Committee noted that some important aspects are missing from the consent form, please review the HDEC template for guidance on missing information.
5. The Committee queried how Maori participants are being supported, noting the significant proportion of sample being Maori. The Committee noted in the current documents this has not been taken into consideration. The Researcher(s) explained that the family members have helped (Maori Academic), who will provide training, on Maori sensitivities. The Researcher(s) noted they would collect ethnicity with census data collection methods, but will not be conducting specific ethnicity data analysis.
6. The Committee note the need to include those with more severe dementia to improve their experience, and acknowledged a case for best interests needs to be made with these individuals in line with right (7)(4).
7. The Committee noted there needs to be a protocol in place to manage A) disclosure of abuse and B) follow up for reports – i.e. the limits of confidentiality. The Researcher(s) noted the possibility for referral to an independent group or body. The Committee acknowledged this was a possibility. Please formalise this arrangement in the protocol.

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

1. Make it clear that this study is for a PhD.
2. The Committee noted any potential negative effects – these should be explained in the Participant Information Sheet, and that the participants are free to express these and their confidentiality will be maintained. Particularly for staff.
3. Add more information to ensure consent is fully informed.

Decision

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

* Please amend the information sheet and consent form, and assent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Observation Studies* *para 6.11*).
* Ethical consideration of studies involving individuals or groups who have diminished competence to give free and informed consent on their own behalf (for example, children) must seek to balance:

a) the vulnerability that arises from the participants’ diminished competence; with

b) the injustice that would arise from their exclusion from the benefits of observational studies in these groups. (See also the Code of Rights, Right 7(3): ‘Where a consumer has diminished competence, that consumer retains the right to make informed choices and give informed consent, to the extent appropriate to his or her level of competence’.)(*Ethical Guidelines for Observation Studies* *para* 6.19)

* Provide cover letter explaining how the study meets legal standards and address outstanding ethical issues raised.

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

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| **5** | **Ethics ref:** | **16/NTA/134** |
|  | Title: | KEYNOTE-355 for Triple Negative Breast Cancer |
|  | Principal Investigator: | Dr Marion Kuper-Hommel |
|  | Sponsor: | MSD |
|  | Clock Start Date: | 01 September 2016 |

Wendy Thomas and Anne Higgins and a Sponsor representative 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.

Dr Charis Brown declared a potential conflict of interest, and the Committee decided to have the member stay in the room but not participate in the decision of the application.

Summary of Study

1. Approximately 860 patients worldwide will be recruited into this 2 parts, Phase 3 study.
2. New Zealand will only be participating in part 2 of the study. Participants must have locally recurrent inoperable or metastatic triple negative breast cancer (TNBC), which has not been previously treated with chemotherapy. Prior treatment with chemotherapy in the (neo)adjuvant setting is allowed.
3. For these participants the period between completion of treatment with curative intent and first documented local or distant disease recurrence must be ≥6 months. Participants who received taxane, gemcitabine, or platinum agents in the (neo)adjuvant setting can be treated with same class anticancer drug (taxane, gemcitabine, or carboplatin, respectively), if ≥12 months have elapsed between completion of treatment with curative intent and the first documented local or distant disease recurrence.
4. Part 1 will be an unblinded, open-label, safety run-in, in which approximately 30 subjects will be partially randomized with forced randomization depending on prior neo) adjuvant treatment, to ensure enrolment of at least 10 subjects to each treatment arm. Subjects will be closely followed for unacceptable toxicities for 21 or 28 days after the first pembrolizumab + gemcitabine/carboplatin or pembrolizumab + taxane administrations, respectively.
5. New Zealand will be participating only in Part 2, which will be a Phase III, double-blind, placebo-controlled study on a background of chemotherapy, for which approximately 828 eligible subjects will be randomized 2:1 to receive pembrolizumab + chemotherapy or placebo + chemotherapy, respectively. Pembrolizumab will be given at 200 mg intravenously (IV) every 3 weeks (Q3W) and normal saline will be used as a placebo.
6. The Researcher(s) explained this is a rare sub type of breast cancer. The treatment options are poor for this patient group.
7. In all 10 participants will be recruited in NZ, in 2 sites

Summary of ethical issues (resolved)

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

1. The Committee stated taking a sample of archival sample should ensure there is sample left, both for clinical purposes as well as participation in other research studies. The Researcher(s) confirmed there is a method to ensure there is sample leftover.
2. The Committee queried how vulnerability would be addressed, due to their treatments being limited. The Researcher(s) stated the discussions that occur between oncologists would outline all treatment options, and all other trials. Furthermore time will be given so they can reflect on participation – and talk with other patient support groups and family.

Summary of ethical issues (outstanding)

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

1. The Committee noted the broadness of the optional sample consent, contrasted with the future biomedical research consent being limited to specific kinds of research. Please justify and explain why the optional sample consent is so broad.

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

1. The Researcher(s) explained future biomedical research is genetic sample. The optional sample is a tumour biopsy, if the patients tumour progresses. The Committee requested a re-write of the optional sample one, as this is not clear at all. Please rename the future biomedical research as future unspecified research.
2. The Committee stated a sole tick box is not acceptable for future unspecified research.
3. The Committee queried the lack of a Māori tissue statement in the Participant Information Sheet. The committee recommended the following statement: *You may hold beliefs about a sacred and shared value of all or any tissue samples removed. The cultural issues associated with sending your samples overseas and/or storing your tissue should be discussed with your family/whanau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult prior to participation in research where this occurs. However, it is acknowledged that individuals have the right to choose.”*
4. The Committee queried the storage of tissue, one has unlimited and one has 20 years. Please specify the time limit, noting that indefinite storage was not acceptable.
5. Add where samples are going in all cases of sending tissue overseas. Make it clear that genetic information is considered potentially re-identifiable.
6. The Committee noted the importance of the language used with regards to identifiability of samples.
7. The Committee queried if the MRI was standard of care. The Researcher(s) explained that these patients would have an MRI for standard of care anyway, however from an investigator point of view all screening involves an MRI. The Committee requested all interventions that are additional to standard of care are made clear to participants.
8. The Committee unclear whether follow up is indefinitely. Please clarify, and make this clear for participants.
9. The Committee queried the additional brochures submitted for this study. The Researcher(s) explained that we usually develop such material in addition to Participant Information Sheet. They will be given to the participants. The Committee noted these must not be used in replacement of the Participant Information Sheet, in particular in relation to future unspecified research. An additional brochure could detract from the Participant Information Sheet. The Committee noted all information about the trial must be in the Participant Information Sheet. The Committee also noted data must be localised for New Zealand audiences.
10. The Committee queried whether there is a second form, as there is a Participant Information Sheet about optional samples, and one for future biomedical research – both talk about genetics, DNA and long term storage. The Committee noted the future biomedical research sheet was much easier to read.
11. The Committee queried how health data (name address phone number DOB) is being used – this will not be sent to the Sponsor, correct? The Researcher(s) confirmed Sponsor would not access any identifiable information. There will be auditors or monitors who will check source files for quality and audit. They are authorised for regulatory purposes. The Committee noted it does not currently read that way. Please revise, make explicit who can access and why.
12. Make it clear what the chances are to receive the study drug versus not getting it.

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 justification for the broadness of the use of tissue for future unspecified research (*Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes, para 2*).

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

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| **6** | **Ethics ref:** | **16/NTA/139** |
|  | Title: | Consolidation of Breast Cancer Registers |
|  | Principal Investigator: | Ms Reena Ramsaroop |
|  | Sponsor: | Breast Cancer Foundation |
|  | Clock Start Date: | 22 September 2016 |

Mr Tony Ryman, and Prof Vernon Harvey 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 Karen Bartholomew and Dr Charis Brown declared a potential conflict of interest, and the Committee decided to have the members stay in the room but not participate in the decision.

Summary of Study

1. The Researcher(s) explained that the four regional registries are running currently. The new combined registry is ready to go live. The data from each register will be extracted and input into the new register. There will be a stage where there will be a hold on data entry.
2. The Researcher(s) explained they are currently testing the IT by using dummy data. The testing will ensure they can map data from one software type to the new software type. The Researcher(s) would like to automate this process.
3. The Researcher(s) explained the software provider have hundreds of registers worldwide.

Summary of ethical issues (resolved)

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

1. The Committee queried how the governance arrangement works. The Researcher(s) noted that they have a current governance group. This new governance is a mixture of the old structures and the new structures.
2. The Researcher(s) noted the makeup of the governance structures, noting there is not a formal board at the moment but there were plans in place for the combined board.
3. The Researcher(s) explained the opt-out process was immediate, rather than the first of January.

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

1. You are encouraged – please reword to ‘we are asking you to’. This ensures impartiality.

Decision

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

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| **7** | **Ethics ref:** | **16/NTA/140** |
|  | Title: | Effects of milk oligosaccharides on the gut-brain axis |
|  | Principal Investigator: | Dr Caroline Thum |
|  | Sponsor: | AgResearch |
|  | Clock Start Date: | 01 September 2016 |

Caroline Thum 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. Human milk is a rich and natural source of complex sugars such as oligosaccharides, which are the third most abundant constituent in terms of concentration after lactose and lipids.
2. Human milk oligosaccharides (HMO) cannot be digested by the human gastrointestinal tract enzymes, and remain, therefore, intact until they reach the large intestine.
3. In the large intestine, milk oligosaccharides enhance the growth of specific bacteria that may affect behaviour. HMOs, for example, can stimulate the growth of specific bacterial genera that have been shown to alter behavioural outcomes, such as reducing anxiety. Colonisation of the infant’s large intestine with detrimental bacteria, however, can activate an inflammatory response that induces depressive-like sickness behaviours and impairs cognition.

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 the study had many aspects that required clarification.
2. The Committee noted the Participant Information Sheet and Consent Form was not an appropriate place to collect data. Please remove any data collection from these documents.
3. The Committee noted the studies scientific validity was problematic, noting there are large confounders, including diet and milk composition,. For example does milk composition change substantially throughout the day. Should scientific validity be problematic then there is an ethical risk of drawing incorrect conclusions from this study.
4. The Committee noted the peer reviewer comments explained that this study is not about the gut-brain axis as there are no measures of brain development of behaviour – it is a descriptive study about matched samples. Therefore, the Participant Information Sheet statements about anxiety and cognition etc. are not part of this study, they are hypothesises for future research, and should be removed or explained as such.
5. The Committee queried whether the study is powered to answer some of the claims, for example b.2.1.
6. The Committee requested a full consideration of Maori, and noted consultation was required as per the Health Research Council Guidelines for Research Involving Maori. Please check with Massy University for guidance. Further it is not acceptable to exclude Maori from the study.
7. This study is not interventional.
8. This study does involve human participants. Because you have stated it does not in the HDEC application screening questions it has resulted in questions not being asked and then answered. Please recomplete the form when you resubmit and ensure the application is filled in correctly.
9. The Committee noted the collection method was problematic. Could you expand the detail on method of collection.
10. The recruitment methods were vague and require clarification.
11. The Committee noted the protocol was very short and overly simple.
12. The Committee noted that the health and demographic data that was being collected was vague and unclear.
13. B.4.4 – data collected would be available to other researchers. This is not mentioned anywhere, nor is it clear in what form with data be provided to others.
14. The Committee noted there is no feedback loop with regards to giving information back to participants, for example a summary of results.
15. R.3.9 – ambiguous around whether tissue was being stored for future unspecified research. States that samples are given numerical identifiers but is unclear what happens to leftover samples. The Committee requires a full explanation about use and storage of tissue.
16. The Committee queried the storage of nappies in the freezer. Please explain if this is appropriate storage.
17. 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.

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

1. The Committee requested a full re-write of the Participant Information Sheet and consent form with reference to the HDEC template. Also an expansion of the Protocol that includes the extra detail requested.
2. Describe all procedures that participants will undergo.
3. The Committee suggests getting a lay member to read the Participant Information Sheet for enhanced understanding.

Decision

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

* Issues relating to Māori cultural and ethical values should be addressed in discussion with Māori concerned (*Ethical Guidelines for Observation Studies* para 4.4)
* The study design must minimise risk of harm (*Ethical Guidelines for Observation Studies* *para 5.5*).
* Please amend the information sheet and consent form, and assent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Observation Studies* *para 6.11*).

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| **8** | **Ethics ref:** | **16/NTA/141** |
|  | Title: | ICON 2 Validation |
|  | Principal Investigator: | Ms Hansinie Laing |
|  | Sponsor: | Fisher & Paykel Healthcare |
|  | Clock Start Date: | 01 September 2016 |

Ms Hansinie Laing and a Sponsor representative were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The ICON 2 is a new platform of integrated humidifier Continuous Positive Airway Pressure (CPAP) devices. The intention of the new platform is to provide a more user-friendly device which encourages acceptance and compliance with CPAP therapy. The purpose of this trial is to validate device performance against participants in an overnight study to ensure the product meets user and clinical requirements.

Summary of ethical issues (resolved)

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

1. The Researcher(s) confirmed this is a product validation study, adding this device is not on the market.
2. The Researcher(s) explained this is a required process before the study can go to market, clarifying this is an internal requirement, but relates to US and EU requirements.
3. The Committee queried whether the proposed pressure decrease was substantial. The Researcher(s) explained it depended on what pressure they were prescribed on, but they would decrease it by a degree of 5. The minimum will be 4cm of water.
4. The Committee queried the qualification of the CI, noting the background was not clinical. The Researcher(s) explained they understand GCP, and have a background of engineering, and there was a clinical team that made up the wider study team.
5. The Researcher(s) explained the volunteer database. They must have formally diagnosed with CPAP and have a device. The Researcher(s) stated they have HDEC approval to store this data for recruitment.
6. The Researcher(s) explained their Maori consultation, adding it has been received.
7. The Committee queried whether this was a clinical study rather than a marketing study, querying the equipoise. The Researcher(s) explained that they need one equivalence study to confirm that the device is equivalent to the old device. The Committee noted this response.
8. The Researcher(s) noted there is no clinical data to suggest that Maori are over-represented with sleep apnoea.
9. R.2.3 – The Committee queried what health information is accessed, is it just prospective or retrospective review. The Researcher(s) stated only data overnight during the study – no retrospective access to clinical notes.
10. P.3.1 – please explain ‘ample time’ – The Researcher(s) stated usually two weeks.
11. The Committee noted that study related procedures should occur prior to ethics approval, referring to sending an email of interest that included study specific information to the registry.
12. The Committee queried how participants will have access to best available treatments post study (page 23 of application). The Researcher(s) explained participants return to standard of care.

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 the peer review is a paid consultant for the Sponsor. The Researcher(s) stated they would arrange an alternative.
2. B.4.4 – The Researcher(s) explained that data is coded against a number, but this is only accessible to the CI and delegated authorities. Any other bodies would receive de-identified data. The Committee requested data storage and future use is clearly explained in Participant Information Sheet.

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

1. Please remove the consent form tick boxes unless the statement is truly optional.
2. Add more information on the sub-therapeutic arm (rationale etc.).

Decision

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

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

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

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| **9** | **Ethics ref:** | **16/NTA/142** |
|  | Title: | Keratin4VLU; A randomised trial |
|  | Principal Investigator: | Dr Andrew Jull |
|  | Sponsor: |  |
|  | Clock Start Date: | 01 September 2016 |

Andrew Jull and Angela X were present in person for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. Leg ulcers are chronic, recurrent wounds and have a major impact of the lives of elders. Most health care for leg ulcers is done in the community, where district nurses alone spend up to a quarter of their time in leg ulcer care. Venous leg ulcers (VLU) are the most common type of leg ulcer accounting for up to 8 out of every 10 people with leg ulcers.
2. VLU can be painful, and limit work, lifestyles and activity. There are few effective treatments for these wounds – compression therapy (tight bandaging or stockings) helps healing, but about half the people with a VLU are "slow healers" even under compression. Standard dressings do not improve healing, but a special class of dressings may speed up healing, especially for people at risk of slow healing. These special dressings are called skin substitutes and keratin dressings are one example.
3. The keratin used in the dressings for trial is derived from New Zealand wool, powdered, treated, freeze dried, and sterile packaged. The keratin from wool dressing appears to stimulate wounds to produce their own keratin, which is necessary to support keratinocytes to migrate and create skin over a wound. The keratin dressings are already in use in New Zealand, the United States and Europe. There is some research to support their use, but not enough to justify change in clinical practice.
4. We intend to use an existing collaborative network of district nursing services to invite patients at risk of slow healing (VLU greater than 5cm2 in area and/or VLU present for more than 6 months) to participate in the trial using the keratin dressing or usual care until ulcer healing. The trial will run for two years.

Summary of ethical issues (resolved)

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

1. The Committee queried how long the bandage is applied. The Researcher(s) stated roughly one week.
2. The Committee commended Participant Information Sheet and the data safety monitoring. The Researcher(s) explained that this population is generally older. They have a data safety monitoring committee to ensure their trial was credible, and to know when to continue or halt the trial.
3. The Researcher(s) explained the increasing prevalence of this disease in younger people, particularly Maori.
4. The Committee queried allergic reaction rate with this product. The Researcher(s) stated they did not know, but it was likely there would be some dermatitis reactions, which they will record.
5. The Committee queried whether researchers would fund GP visits that were as a result of an allergic reaction. The Researcher(s) stated no funding available. The Committee noted ACC would be possible to apply for participants, but that participants would need further support to actually follow that claim through and get to the GP.
6. The Committee requested Pacific ethnicity could be considered as sub groups, rather than generalising. The Researcher(s) explained that they ask participants to self-identify all ethnicities.
7. The Researcher(s) confirmed co-morbidities are being collected.
8. The Researcher(s) noted that this is also a disproportionate problem for Asian communities, and noted our dataset will be available or re-analysis to ensure the information is used for many other ethnic groups.

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

1. Remove yes or no options unless they are truly optional. The Committee noted adverse event is not a lay language term.
2. Add full disclosure on who provides the dressing for the study.

Decision

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

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| **10** | **Ethics ref:** | **16/NTA/144** |
|  | Title: | Dyspnoea during exercise |
|  | Principal Investigator: | Dr Kevin Ellyett |
|  | Sponsor: |  |
|  | Clock Start Date: | 01 September 2016 |

Kevin Ellyett 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. Breathlessness (dyspnea) during exercise is common in adolescence. This exercise induced dyspnea (EID) can become a barrier to participating sports and other exertional recreation. This barrier has the potential to influence lifestyle choices into adulthood. Additionally, it is not uncommon for individuals who experience EID to be diagnosed with asthma and treated as such, albeit that they are not asthmatic.
2. One probable cause for the observed EID in non-asthmatic adolescence is expiratory (air) flow limitation (EFL). EFL occurs when the generated flow out of the lungs exceeds its physiological limitation. EFL generally occurs in individuals with pathologies that affect the airways such asthma or chronic obstructive pulmonary disease. However EFL can occur in a normal subject and can be caused primarily by one of two mechanisms. Firstly adoption of a breathing pattern that generates high flows during expiration which exceeds that maximum capacity of the system and causes EFL. Secondly if the ratio airway diameter to lung volume is low (which is normal in adolescence and more common in females c.f. males) the volume air needing to be moved per breath is greater than that which the airways are capable of facilitating and this too will induce EFL. Albeit these two mechanisms are distinct they can also combine to exacerbate EFL during exercise.
3. If EFL is reached during exercise EID occurs and increased exertion is limited. This is abnormal in younger people as the predominant limiting factor for maximal exertion is generally the cardiovascular system.
4. This study aims to determine what proportion of adolescent girls who self-report EID are EFL during exercise. This will allow for a better understanding of the prevalence and aetiology of EFL in this group, which will lead to an improved management and awareness of this condition.

Summary of ethical issues (resolved)

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

1. The Committee queried whether death is a risk for the cardio pulmonary exercise for this population. The Researcher(s) explained the risk of death exists in literature, though is associated with adults who have other comorbidities. The Committee noted this response.
2. The Researcher(s) noted that the peer review is independent from the study.
3. The Researcher(s) noted consultation would occur in line with ADHB locality processes.
4. The Researcher(s) explained the theory behind the over diagnosis of asthma, adding this assumption is why they include those who have a diagnosis, as if they were excluded they would actually be excluding some of the people we are wanting to see. The Researcher(s) noted that only 20% of asthmatics actually demonstrate flow limitation during exercise, explaining they get the asthmatics to take their treatment prior to the study.
5. The Researcher(s) confirmed they are not aiming to determine the number of people who have been misdiagnosed with asthma. The Researcher(s) noted obstructive airway disease is an exclusion criteria.
6. The Committee noted sub-group analysis for Pacifica is important, if not for this study but for future research.
7. The Committee noted that health information should be stored for 10 years from the date a child turns 16.
8. P.1.1 – The Committee noted consent should be given before any study procedures. The Researcher(s) confirmed they would.

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 they would need to see a more detailed recruitment plan, including any advertising.

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

1. The Committee stated there needed to be a range of participant information sheets for the various age groups:

Rules:

At 16 a person can consent to participate. Even so – they may need a very well written information sheet in lay language to understand, and simple language should be used.

Under 16 some may be competent to provide consent. Most will provide assent, with consent given by legal guardian.

Guidance:

When you have participants that are under 16 they need age appropriate written material to help them understand. The age groupings are somewhat irrelevant, as it is a person’s capacity that determines the level of information that should be given to them.

Some children who are under 16 may be competent to provide their own consent.

The best practice for a study involving children and adults would be to have:

* An adult participant information sheet. This is for anyone providing consent. This means it can be used by a participant who is 15 if it is determined that they can understand it.
* A shorter, simpler, participant information sheet. This is used for adolescents to provide assent. It would support a verbal discussion about the study. The age range could be 13-15. It can also be used for competent 12 year olds, for instance.
* There should also be the adult PIS/CF. This can be more or less the same as the 16 and over document, but it refers to ‘your child’ rather than ‘you’.

1. Add travel time; explain what child will be required to do and length of time it will take (in parent Participant Information Sheet).
2. Add ACC compensation statement: *“If you were injured in this study, which is unlikely, you would be eligible* ***to apply*** *for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery. If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.”*

Decision

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

* Please provide age appropriate information sheets and assent forms for younger participants and amend the existing information sheets and assent/consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Provide details on what processes are in place to accommodate recruitment *(Ethical Guidelines for Intervention Studies para 6.2).*

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

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| **11** | **Ethics ref:** | **16/NTA/146** |
|  | Title: | PREDICT KT Study |
|  | Principal Investigator: | Dr Stuart Dalziel |
|  | Sponsor: |  |
|  | Clock Start Date: | 01 September 2016 |

Dr Stuart Dalziel and Libby Haskell were present in person for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. Bronchiolitis is the commonest lower respiratory tract infection in children less than 12 months and the most frequent cause of hospitalisation in infants under 6 months of age in Australasia. Treatment is well defined and consists solely of supportive therapies such as supplemental oxygen and fluid replacement. Despite this, substantial variation in practice occurs.
2. Guidelines contain systematically developed statements that help practitioners and patient decision makers decide on appropriate health care for specific clinical circumstances. Further, guidelines offer explicit recommendations for clinicians, influence the beliefs of healthcare providers and practitioners accustomed to outdated practices, improve the consistency of care, and provide authoritative recommendations that reassure practitioners about the appropriateness of their treatment plan.
3. The aim of this study is to answer the question: In infants presenting to Emergency Departments (EDs) and admitted to inpatient settings with bronchiolitis, does tailored, theory informed Knowledge Translation (KT) interventions increase the uptake of an Australasian Bronchiolitis Guideline in reducing the use of therapies/management known to be of no benefit in infants with bronchiolitis? This will be done by randomising hospitals to either intervention or control. Results from this study will influence the successful implementation of other guidelines and evidence based practise in paediatric settings.

Summary of ethical issues (resolved)

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

1. The Researcher(s) explained the history of treatment for bronchiolitis, and noted how difficult it was for patients to receive correct care, as treatment is provided when it is not required.
2. The Researcher(s) noted they have audited 600 patients at their own practice to check how much they were over treating in relation to reported percentages in literature.
3. The Researcher(s) explained that this study is about developing evidence based guidelines. The guidelines are 150 pages long, developed with 20 individuals across New Zealand and Australia.
4. The Researcher(s) are going to randomise whole centres – one site will put guidelines up on their intranet, as is usual for new guidelines, and the intervention arm will have more intensive training. The Researcher(s) explained that the protocol is vague to ensure there is not a hawthorn effect.
5. The Committee noted this intervention is to change clinician behaviour to impact their treatment delivery.
6. The Committee noted that the data is being accessed to check whether the practitioners are following the guideline or not. The hospital level checking already occurs as audit related activities. The Committee noted the randomisation is effectively a quality control measure.
7. The Researcher(s) noted HRC funded this project.
8. The Committee noted why the data was stored off site.
9. The Researcher(s) note that after one year the study will determine what works better, and will offer that training package to all participating hospitals.
10. The Committee noted collecting subgroup ethnicity would be preferred for future analysis. The Researcher(s) noted data is not collected prospectively, it is all accessed in a de-identifed form retrospectively.
11. The Committee noted that hospital data is accessed to determine adherence to the guidelines. There is a great public value and all data is de-identified. The study is randomised at the system level, and involves educational initiatives, and that the data of patients do not make them the participants.

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

1. Explain that the study involves PhD in the staff Participant Information Sheet.

Decision

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

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| **12** | **Ethics ref:** | **16/NTA/148** |
|  | Title: | The SPACE Trial |
|  | Principal Investigator: | Dr Natalie Walker |
|  | Sponsor: | The University of Auckland |
|  | Clock Start Date: | 01 September 2016 |

Dr Natalie Walker 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. Smoking remains the leading cause of COPD, a leading cause of death and disability in New Zealand. COPD particularly affects Māori and Pacific people, given their higher rates of smoking. COPD patients tend to have a higher level of nicotine dependence and, as a result, often find quitting harder and are more likely to relapse back to smoking.
2. A clinical trial (N=262) is planned in Auckland to determine whether extended varenicline treatment combined with behavioural support can prevent relapse back to smoking in recent ex-smokers with COPD. Other outcomes of interest include changes in lung function and quality of life. Smoking cessation and relapse prevention are the most cost-effective interventions available for COPD patients that smoke, irrespective of their disease stage.
3. The trial has the potential to significantly improve the outcomes of this common and chronic health condition in New Zealand. It is HRC funded

Summary of ethical issues (resolved)

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

1. The Committee queried if everyone who manages to quit will go onto the second phase. The Researcher(s) stated only the required number will go on to the second phase. The Committee queried what happens to the people who quit when the study sample sizes are full for phase two. The Researcher(s) noted they will be supported, but not included in the study, as if we over recruit it will be unethical.
2. The Committee noted insurance out of date. Researcher apologised, stating they had noticed that just before the meeting
3. Make clear other interventions are accessible post study.
4. The Committee noted that a $10 food voucher may not provide the support required to facilitate transport to and from the study clinic for the most vulnerable populations.
5. The Committee noted $5 (pharmacy fee) may be a potential barrier for some, noting it has been found that for some of those most vulnerable it can be a struggle to pick up their prescription. Please look into measures to enhance access to study clinic and getting the prescription, to facilitate equitable access to the study by all.
6. The Researcher(s) and Committee discussed COPD rates in Maori.
7. The Committee queried why the participants need to pay for the treatment, noting the large grant from HRC. The Researcher(s) noted the government heavily subsidises medication for patients – to access it any other way would be very expensive. It also replicates the real world data. The Researcher(s) clarified the treatment is administrated by special authority.
8. The Researcher(s) confirmed they have a study doctor who can provide special authority prescriptions.
9. The Committee queried how they will identify potential participants. The Researcher(s) stated advertising.
10. The Committee queried whether the participants received access to best intervention post study. The Researcher(s) stated that the study drug is best medication that New Zealand has to offer. At the end of the study, if the participants have not quit, the researchers can offer the study drug again, or offer different drug. The Researcher(s) confirmed they will give participants the prescription that they want to try and quit. The Researcher(s) confirmed they can get in touch with GP if permission given by participants and there are other behavioural / counselling options too.
11. The Committee queried whether the participants are vulnerable, noting application stated they were. The Researcher(s) explained yes in a sense they are vulnerable, they have a terminal illness, that kills slowly, and they may be addicted.
12. The Researcher(s) explained Participant Information Sheet given to possible participants for about a week to consider participation.
13. The Researcher(s) explained that this drug is not indicated for relapse prevention.
14. The Researcher(s) confirmed creator of drug is not involved at all.
15. The Researcher(s) noted they can seek other treatment during the study, the researchers will add to data and take into account, noting this was a pragmatic design.

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

1. Add ‘verbal’ to support.
2. The Committee requested that it is clear on the Participant Information Sheet that if you quit you may not get onto second part of the study.
3. Please remove yes or no tick boxes, unless statement is truly optional.
4. Explain placebo in lay terms.
5. Add: *“If you were injured in this study, which is unlikely, you would be eligible* ***to apply*** *for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery. If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.”*
6. Add more generic numbers in event of suicidal ideations.
7. Make sure the information in the brochure is in the Participant Information Sheet.

Decision

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

## General business

1. The Committee noted the content of the “noting section” of the agenda.
2. The Chair reminded the Committee of the date and time of its next scheduled meeting, namely:

|  |  |
| --- | --- |
| **Meeting date:** | 11 October 2016, 01:00 PM |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

1. **Problem with Last Minutes**

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

The meeting closed at 6.30pm