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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 08 September 2015 |
| **Meeting venue:** | Novotel Ellerslie |

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| **Time** | **Item of business** |
| 1.00pm | Welcome |
| 1.15pm | Confirmation of minutes of meeting of 11 August 2015 |
|  | New applications (see over for details) |
| 1.30pm | i 15/NTA/117  ii 15/NTA/119  iii 15/NTA/120  iv 15/NTA/121  v 15/NTA/122  vi 15/NTA/123  vii 15/NTA/126  viii 15/NTA/128  ix 15/NTA/129  x 15/NTA/130  xi 15/NTA/131  xii 15/NTA/132 |
| 6.30pm | Substantial amendments (see over for details) |
|  | i 14/NTA/100/AM07 |
|  | General business:   * Noting section of agenda |
| 6.45pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Brian Fergus | Lay (consumer/community perspectives) | 01/07/2012 | 01/07/2015 | Apologies |
| Ms Susan Buckland | Lay (consumer/community perspectives) | 01/07/2012 | 01/07/2015 | Apologies |
| Mr Kerry Hiini | Lay (consumer/community perspectives) | 01/07/2012 | 01/07/2015 | Absent |
| Ms Michele Stanton | Lay (the law) | 01/07/2012 | 01/07/2015 | Present |
| Dr Karen Bartholomew | Non-lay (intervention studies) | 01/07/2013 | 01/07/2016 | Present |
| Dr Christine Crooks | Non-lay (intervention studies) | 01/07/2013 | 01/07/2015 | Present |
| Mr Mark Smith | Non-lay (intervention studies) | 01/09/2014 | 01/09/2015 | Present |
| Ms Shamim Chagani | Non-lay (health/disability service provision) | 01/07/2012 | 01/07/2015 | Present |
| Mrs Helen Walker | Lay (consumer/community perspectives) | CEN – Co-opt | CEN – Co-opt | Present |

## Welcome

Note: Dr Brian Fergus was absent for the meeting and Mrs Helen Walker has been co-opted to Chair the meeting.

The Chair opened the meeting at 1.07pm and welcomed Committee members, noting that apologies had been received from Dr Brian Fergus and Ms Susan Buckland.

The Chair noted that the meeting was quorate.

The Committee noted and agreed on the agenda for the meeting.

## Confirmation of previous minutes

The minutes of the meeting of 11 August 2015 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **15/NTA/117** |
|  | Title: | Oxygen in Acute Coronary Syndromes |
|  | Principal Investigator: | Prof Ralph Stewart |
|  | Sponsor: |  |
|  | Clock Start Date: | 27 August 2015 |

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

Potential conflicts of interest

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

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

Summary of Study

1. The study investigates the question ‘what amount of oxygen should be given to patients presenting with a heart attack’.
2. The Researcher(s) explained that currently patients are routinely given oxygen through a high flow mask, regardless of the oxygen level in their blood, as they know heart attacks are caused by blockages in the arteries in the heart. Part of a heart attack can involve a lack of oxygen going to the heart. However recently there is evidence to suggest that additional oxygen may either not provide a benefit or may cause harm (potentially increase the size of the infarct). The Researcher(s) explained they have no statistically valid information in the real world, in patients, as to whether the amount of oxygen makes a difference – favourable or not.
3. The Researcher(s) explained that there is clinical equipoise between the two arms of the study (two different protocols of oxygen administration), with local practices enacting different protocols within New Zealand (this may be clinician dependent). If there is a real difference between the two protocols (eg current practice is shown to have a negative impact on heart attack outcomes), the effect eg on length of stay in hospital, and on mortality between the protocols administered are likely to be modest. However a difference of only 1% in mortality will be hugely valuable clinically, and has the potential to save a large number of lives over time. Therefore a large study must be conducted to know what works better for patients and answer the question definitively.
4. The Researcher(s) explained the different kinds of presentations that occur with patients and how the oxygen protocols are different.
5. The Researcher(s) stated they would recommend one of two oxygen protocols, which will be the default protocol, for a standard period of time. The arms (network geographic location containing hospital and community sites) will cross over protocols and over time. This design ensures that the study data is valid. Randomised oxygen protocols will be adhered to in ambulance settings, the Emergency Department and coronary cath lab services. All hospital sites in the national cardiac network have agreed to participate, so effectively the intervention will be applied to anyone in New Zealand who has a heart attack over the study period.
6. What is being compared is a health care delivery intervention of two different oxygen protocols for heart attack patients – one where all patients get oxygen regardless of their oxygen status, and the other where oxygen delivery is titrated based on a specified blood oxygenation level (measured by a routine and non-invasive technology the oxygen saturation monitor).

Summary of ethical issues (resolved)

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

1. The Researcher(s) explained that in this case (environment) – what we are doing is recommending a default oxygen protocol be used. This is done by the whole ‘system’ being involved in the study. The Researcher(s) want to standardise oxygen delivery practice with evidence-based guidelines, in order to provide maximal health outcome benefit for patients. To do this they will formalise both protocols which are in current practice and randomise the whole system to one or other of these.
2. The Researcher(s) noted the primary ethical issue is that they propose not to seek individual consent. Their rationale for this is as follows:
   * The study is a health care delivery, best practice, quality improvement intervention and is also effectively a ‘whole of system’ community intervention, although it is randomised.
   * At the point of care patients would have reduced competence to provide informed consent due to chest pain and anxiety, as well as other contributing factors. It would also be impractical to seek consent at this time, were a patient competent to provide it, due to the acute nature of the condition and the time critical nature of access to hospital level treatment.
   * It would be impractical to individually consent the sample size required to determine a clinically significant difference between the two oxygen protocols.
   * Information about the study is provided and easy to access at all participating sites (eg posters) allowing openness of information about the study. Further information is also presented on the internet. Further information will be available to patients or their families (eg a brochure).
   * Patient autonomy is protected because information is provided and they can opt out (remove their data) if they wish.
   * Clinical opinion can override the oxygen protocol at any time deemed necessary. Analysis will be by intention to treat.
3. The Committee explained right 7(4) of the Code of Rights; with a focus on whether the intervention is in the patient’s best interests. The potential benefit is standardised practice and better outcomes for patients. The Researcher(s) proposed that both protocols are in the patient’s best interest in that each protocol is regarded as equally reasonable, clinically. Many protocols in current practice have not been appropriately evaluated – this is a real issue in standard of care, and will only be addressed by studies like this.
4. The potential harms are very minimal to non-existent. Only a very small aspect of clinical care is being varied, and it is variation that currently exists in usual practice. All other aspects of care will be clinically determined and not affected by the oxygen protocol used.
5. The Researcher(s) added that if the study determines that one protocol is better than the other the study will be stopped and standard of care will be altered.
6. The Committee asked where the two types of oxygen protocols are used. The Researcher(s) stated that oxygen was commonly administered – even if level of oxygen is normal, a mask is usually given to patients. However many cardiologists are moving away from this practice, with their care moving towards not giving oxygen, based on the level of oxygen in the blood, and instead giving air.
7. The Committee asked where the protocol(s) are used around New Zealand. The Researcher(s) stated care is often not given within a protocol - it is given as care, based on clinician preference.
8. The Researcher(s) stated that giving oxygen only when oxygen saturations are low is now present in some European guidelines.
9. The Committee asked about previous research. The Researcher(s) noted that it was suggestive of better outcomes for the limited oxygen arm, but results were limited by the small study size. Differences were borderline, not clinically significant to provide a definitive answer. Change in practice will be driven by evidence of clinically relevant difference between the oxygen protocols, for example in mortality.
10. The Committee asked why infarct size isn’t a measure in the proposed study. The Researcher(s) stated it would be a good secondary measure but it can’t be measured reliably in usual care. Primary clinical endpoint is mortality, with secondary end points being clinically relevant proxy indicators such as length of stay or clinical scores.
11. The Researcher(s) stated the study would involve all patients who have a heart attack over a two-year period.
12. The Committee noted the Swedish study referenced in the Protocol involved all participants’ providing consent (6000 participants). The Researcher(s) stated that this would not answer the clinical question this study was designed to answer for two reasons:
    * The sample size is not big enough to detect the likely modest mortality end point ie even if a difference was found this evidence would not be definitive enough to change practice.
    * That people who consent to the study are those able to provide informed consent and therefore will exclude all those too sick. In recent research on the Swedish heart registry it was demonstrated that the mortality difference between these two different groups of patients was approximately 10% ie the two groups were so different that the potential application of the study results to the whole population was extremely limited. This is a statistical bias that the researcher(s) want to avoid to be able to provide generalisable results.
13. The Researcher(s) stated if this (Swedish) study did show a clinically important and statistically significant result that one oxygen protocol was better than the other, then our study would be stopped.
14. The Committee queried if legal advice had been sought. The Researcher(s) stated no. The Committee suggested seeking legal advice on the trial. The Committee noted that NEAC Guidelines require trials to be legal, even if ethical.
15. The Committee queried if because the study is multi site whether there will be protocols in place to ensure patient safety. The Researcher(s) stated they would – it would primarily be the use of a recommended protocol that is given to all relevant clinicians. The Researcher(s) added that clinicians remain able to override the oxygen protocols at any point based on their clinical opinion.
16. The Researcher(s) confirmed the study is supported nationally by clinicians in the cardiac network. The study is funded by the National Heart Foundation and Health Research Council Data Safety Committee have agreed to act as the independent data safety monitoring committee.
17. The Committee queried why such large numbers of participants are needed. The Researcher(s) stated that this is due to the mortality end point and the likely very most effect (if any), the study therefore has to have a large sample size to provide sufficient statistical confidence in the result. The independent DSMC would look at data while it is collected so it can be stopped early if a definitive answer is determined
18. Committee summarised the study, noting the gold standard protections in place for participants. This is consistent with the NEAC Guidelines on Interventional Studies (5.53, 6.16, 6.26) and the HRC guidelines (2005) on healthcare and community interventions (page 15 and 17). The committee noted study could be stopped if a definitive outcome for which oxygen protocol would be recommended is found. The Committee noted a legal opinion should be sought. The Committee noted best interests are met by the fact that both are standards of care and the risk of harm is very low with the clinician opinion overriding the protocol.
19. The Committee asked when DMC is meeting. The Researcher(s) stated it would be meeting in 1 month (from today) then meeting regularly (every 4 months once study commences).

Decision

This application was *approved* by consensus. HDEC noted the need to submit first DSMC reports to continue on-going ethical approval.

HDEC is to be advised of legal outcome.

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| **2** | **Ethics ref:** | **15/NTA/119** |
|  | Title: | A4091058 (Pfizer OA) |
|  | Principal Investigator: | Dr Simon Carson |
|  | Sponsor: |  |
|  | Clock Start Date: | 27 August 2015 |

Dr Simon Carson (Co-ordinating Investigators) and Pfizer representatives - Ms Selene Og, Ms Amy Burr and Mr Bob Fountaine were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of ethical issues (resolved)

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

1. The Committee noted the response letter to the issues raised in the decline by the Southern HDEC. The Committee considered the researcher adequately addressed the issues raised by the Southern HDEC. The Committee noted there were further issues that needed to be addressed prior to full approval
2. The Committee queried whether there was any additional risk of infection, noting the use of biologics. Are prophylactic antibiotics necessary? The Researcher(s) stated there is no reduction in immune system function, and no additional risk of infection, other than normal risks associated with administering treatments.

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 samples should not be kept indefinitely and requested acceptable end point for storage.

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

1. Please make it clear that participants don’t need to answer all questions on questionnaires (page 15.)
2. The Committee asked why there was a optional consent to the joint fluid sample being included in the study at the end of the consent form (page 22) noting there was no information in the Participant Information Sheet about these samples? The Researcher(s) stated joint aspiration is a clinical practice for relief of symptoms at the discretion of the treating clinician (not part of the study protocol), and that the sponsor would like request consent to obtain samples to analyse (for PK/PD), if this occurs. The Committee requested this information is added to the Participant Information Sheet to explain this for participants.
3. Purpose of research study – second paragraph. The Committee noted there are three options for NSAIDs (naproxen, celecoxib, or diclofenac). Please name the drugs at the beginning of the Participant Information Sheet.
4. Add information on cultural issues (with tissue etc.) from optional tests to main Participant Information Sheet, common standard text is:
   * 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 Maori 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.
5. HIV test wording ‘The HIV tests are required unless not allowed by health authorities in New Zealand (per local guidelines)’. Please localise to the New Zealand context, including notification of site practice for management of positive results for either HIV or hepatitis (eg appropriate notification pf participants, mandatory laboratory notification of health authorities and GP or specialist referral).
6. The Committee noted RMI guidelines is now out-of date – please view Medicines New Zealand website for information on correct title of industry guidelines.
7. For the main study PISCF and optional PISCF be more specific about where samples will be stored internationally, and provide a reasonable length of time for storage (indefinite or “no time limit” is not acceptable as noted above). Please ensure all requirements outlined in the Ministry of Health Guidelines for Future Unspecified Research are met (http://www.health.govt.nz/publication/guidelines-use-human-tissue-future-unspecified-research-purposes-0 )
8. Explain whether incidental findings or clinically significant results will be relayed to donators. The Researcher(s) stated standard practice is to send anything clinically relevant back to participants. The Committee noted this does not appear to be standard for sub-study future unspecified research and tissue testing. Researcher(s) to clarify for the Committee and to participants.
9. Please reconsider use of word ‘drop out’. Participants must be carefully managed.
10. Page 19 – Access to Medical History - ‘may need to access’ change to ‘will need’.
11. Paragraph 3, page 1 – on Optional Participant Information Sheet “optional request and you do not have to agree to this request even if you are providing specimen(s) add…’for the main study.’
12. Remove the options for initials on page 2. Add these to the consent form for the optional Participant Information Sheet.
13. The Committee queried whether it was clear to participants what being ‘a control’ was. (page 2, Optional Participant Information Sheet). This appears to be a significant extension to the broad consent for sample use relevant to chronic pain, into blanket consent for any kind of research. Please be clearer about what this means to participants so that they can make a fully informed decision.

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Please provide a limit on storage of human tissue.

This following information will be reviewed, and a final decision made on the application, by Dr Mark Smith and Ms Michelle Stanton.

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| **3** | **Ethics ref:** | **15/NTA/120** |
|  | Title: | Evaluating the effect of a new drug on exercise tolerance in subjects with angina |
|  | Principal Investigator: | Prof Russell Scott |
|  | Sponsor: |  |
|  | Clock Start Date: | 27 August 2015 |

Dr Jinny Willis and Prasanna Karunasekera (Study Co-ordinator) 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 Researcher(s) explained that study drug is being developed to treat migraines. The Researcher(s) explained that the study drug has vascular effects and so needs to be investigated in patients where this may be problematic eg angina. The research will investigate whether the study drug impacts exercise tolerance in patients with stable angina.
2. The Researcher(s) explained that the screening involves exercise-screening tests. If the participants meet certain parameters they will have one infusion of study drug. Participants will then be followed up, including blood tests and questionnaires.

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 questionnaires on suicidal ideations. The Researcher(s) explained the FDA requirements (on drugs that impact the brain). This is a non-binding recommendation. The Researcher(s) noted information on the FDA requirements is also in the ethics submission.
2. The Committee queried what occurs if the questionnaire scale results in an identified increased risk of suicide. The Researcher(s) explained that while there is no evidence that the drug will cause any suicidal ideations, they have an established pathway involving training. Clinicians have follow up plans, involving referrals to psychiatric services.
3. The Committee noted SCOTT review is pending.
4. The Researcher(s) noted participants will not benefit from the drug, but explained that this is like phase I studies in healthy controls (ie non therapeutic).
5. The Researcher(s) noted that a potential benefit results from angina patients having an exercise test, but noted this is a minor benefit, perhaps outweighed by the risk of the test itself (outlined in the PIS and application)
6. The Committee asked if PK and biomarker testing is compulsory. The Researcher(s) confirmed it was.
7. The Committee asked if genetic testing is part of the biomarker testing. The Researcher(s) stated there was no genetic testing involved.
8. The Committee noted people needed to know what is happening with their tissue samples. See HDEC template Participant Information Sheet for guidance.
9. Add information about what actually occurs when participants withdraw from the study, and what happens to their samples. The Committee noted participants should be able to withdraw their samples and this should be clearly stated.

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 confirmation that there is no optional future unspecified research involving human tissue or genetic sampling.

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

1. Explain the suicidality parameters where these are first mentioned (page 5). Currently insufficient information around why these are necessary and how any positive screen will be managed.
2. The Committee noted there are significant risks involved with treadmill tests. The Committee expects that there are full resuscitation kits and suitably trained observing clinicians (not just “caregivers” as stated in the PIS). The Researcher(s) noted this test would occur in hospital cardiac setting (this assurance of appropriate risk management for the test itself would require particular consideration in the Localities Approval process). The Committee explained that the safety features to manage this risk should be added to the Participant Information Sheet.
3. Please be consistent when referring to the treadmill test. It is currently referred to in a variety of ways.
4. Please include information on where tissue samples are going. The Researcher(s) explained that because this study is being undertaken in a number of studies they are using a centralised laboratory. Please add information on samples going overseas under a section termed ‘what happens to my samples’. Including length of time of storage.
5. The Committee noted the Participant Information Sheet does not adequately convey that this is a non-therapeutic study, and that there is no benefit for study involvement. It must be very clear that the potential for benefit is for A) future people and B) a different patient population.
6. The Committee noted that the descriptions of ‘tests outlined in the protocol’ and ‘for safety follow up’ is not sufficient information regarding the testing of samples. Blood tests, biomarker development and PK testing must be explained in lay language.
7. Review the use of jargon throughout the PIS (for example “sublingual nitro-glycerine”.

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*).
* Confirm there is no future unspecified use of tissue or biobanking.
* If there is biobanking - please provide a separate Participant Information Sheet and Consent Form for the use of tissue for future unspecified research and an overview of the research and information on the tissue bank (*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 Ms Shamim Chagani and Ms Helen Walker

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| **4** | **Ethics ref:** | **15/NTA/121** |
|  | Title: | A4091064 (Observation) |
|  | Principal Investigator: | Dr Simon Carson |
|  | Sponsor: | Pfizer Australia/New Zealand |
|  | Clock Start Date: | 27 August 2015 |

Dr Simon Carson and Bob Fountaine a medical expert from Pfizer were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of ethical issues (resolved)

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

1. The Committee queried why there were only 250 participants out of 3000 in parent study. Who is patient population for this, and how are people selected? The Researcher(s) stated people who will undergo total knee, hip or shoulder replacement.

Summary of ethical issues (outstanding)

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

1. Page 2 Participant Information Sheet – The Committee noted that there could be medical risks for participants undergoing surgery, if participants and clinicians remain blinded to prior treatment post parent study. Please provide evidence on the lack of additional risk to participants. The Researcher(s) stated previous studies show no difference in risk. Please provide a justification of not un-blinding, and provide additional safety protocols for emergency unblinding in cases of adverse event. Local orthopaedic clinical opinion may also be useful.
2. R.3.12 – states retaining tissue slides indefinitely. Please provide a limit to length of storage, with a rationale.

Decision

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

* Please justify maintaining the study treatment blind, and explain how any resulting risks will be managed. The study design should be the one best suited to answer the study question, while minimising harm, maximising benefit and meeting other ethical standards. (Ethical Guidelines for Intervention Studies para 5.4).
* Please provide a limit on storage of human tissue.

This following information will be reviewed, and a final decision made on the application, by Dr Mark Smith and Ms Michele Stanton.

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| **5** | **Ethics ref:** | **15/NTA/122** (CLOSED) |
|  | Title: | Drug Interaction Study between an experimental Hepatitis C treatment and an oral contraceptive drug. |
|  | Principal Investigator: | Dr Richard Robson |
|  | Sponsor: | Gilead Sciences ANZ |
|  | Clock Start Date: | 27 August 2015 |

Dr Chris Wynne 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.

Decision

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

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| **6** | **Ethics ref:** | **15/NTA/123** |
|  | Title: | ASCEND-II |
|  | Principal Investigator: | Dr Natalie Walker |
|  | Sponsor: | The University of Auckland |
|  | Clock Start Date: | 27 August 2015 |

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. The study will assess whether e-cigarettes with and without nicotine, in combination with standard treatments (patches) can assist people with quitting smoking.
2. The Researcher(s) explained that the Ministry of Health need information to regulate e-cigarettes.
3. The study is a 3 arm-trial and will assess smoking cessation and effectiveness of each arm in sustained quitting.

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 participants would be identified and the consent processes in place. The Researcher(s) stated the primary method would be community based advertising. The Researcher(s) explained that past studies indicate that there would be no problem getting participants. The Researcher(s) stated there is a phone number people can contact if they see their advertising. Consent is verbal, and the script is provided.
2. The Committee noted information sheets are emailed or posted to participants.
3. The Researcher explained how the device (E-cigarette) could be highly personalised. Users can manage how much nicotine they receive – this is different to the constant but low dose administered with patches.
4. The Committee queried why there was no e-cigarette and no patch study arm, noting an HRC reviewer also asked this question. The researcher(s) noted that a four arm study would be complex and that their interest (and the Ministry of Health) is in the potential additive effect of the e-cigarette to the current standard treatment of patches.
5. The Committee asked about the consent to future re-contact for potential sub-studies. The Researcher(s) stated these are just placeholders, explaining they would come back to ethics for any further studies. The Researcher(s) confirmed that the Participant Information Sheet had information on approaching existing participants for further, related research.
6. The Committee asked if there is a standardised questionnaire used to talk to smokers about their use. The Researcher(s) stated no – the information is collected with study specific questions.

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 about consent and screening. The Committee noted that verbal consent should be sought before collecting screening information. Informed consent generally occurs prior to any study related procedures. The Committee suggested a staggered (2 step) consent process, where permission is sought to continue with screening (and documented), and then informed consent for the main study is sought after successful screening. Please amend protocol.

Decision

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

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| **7** | **Ethics ref:** | **15/NTA/126** |
|  | Title: | Antibiotics in critically ill children (Part A) |
|  | Principal Investigator: | Dr Brian J Anderson |
|  | Sponsor: |  |
|  | Clock Start Date: | 27 August 2015 |

Jacqueline Hannam (co-investigator) was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The study investigates antibiotic use in 0-18 year olds. Hypothesis is that current practice is potentially under dosing antibiotics.
2. The Researcher(s) explained that the overall aim is to come up with a model that will rationalise our dosing, to improve the way we treat children with antibiotics.
3. This is one of two similar studies; the other is in post-operative children who will be pre-operatively consented.

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 there are any specific risks with the younger participants - babies or very young infants. The Researcher(s) stated no, not to their knowledge. The Researcher(s) explained that the main problem is that they can’t consent. The Researcher(s) stated they would seek parental consent and are aware that there will be sensitivity for the parents that may impact on their ability to consent due to their child being seriously unwell.
2. The Committee noted that the study is observational.
3. The Committee queried whether the reviewer comments regarding active exclusion criteria of participants who have additional bleeding related risks. The Committee noted that all participants will already have a IV port, so any bleeding issues will be reduced. The Researcher(s) stated that was correct.
4. Please note that health data derived from the study must be stored for a minimum of 10 years once the child turns 16 years according to the [Health (Retention of Health Information) Regulations 1996](http://legislation.govt.nz/regulation/public/1996/0343/latest/DLM225650.html).
5. The Committee queried who approaches and consents participants. The Researcher(s) noted that it is whoever is on the ward at the time. The Committee noted potential coercion due to parents agreeing with their doctor, who is treating their sick children. The Researcher(s) stated they could use a research nurse instead. The Committee noted this is appropriate.
6. The consent and assent cascade of age appropriate documents was noted to be well done, and the researcher was thanked for the effort in customising these for the appropriate audience.

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

1. Change to ‘you’ to ‘your child’ on the parent Participant Information Sheet.
2. Add information about the right to withdraw and the right to access participant’s health information.
3. Add information on length of time data is stored as above.
4. Add information on the sample testing, where they will be stored, the length of time kept and how they will be destroyed.
5. Add that the study has the potential for future benefit for future children.
6. Seek separate consent to access medical records and blood test results. Add on consent form.

Decision

This application was *approved* by consensus.

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| **8** | **Ethics ref:** | **15/NTA/128** |
|  | Title: | IPI-145-06 |
|  | Principal Investigator: | Dr Peter Ganly |
|  | Sponsor: | Infinity Pharmaceuticals, Inc. |
|  | Clock Start Date: | 27 August 2015 |

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. Four participants in New Zealand from 120 worldwide.
2. The Committee noted the study has a data safety monitoring committee.
3. The Committee noted the study is seeking SCOTT review.

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 what would happen to tissue samples. Please provide an overview of what happens to samples. Will tissue (and health data) be stored indefinitely? The Committee noted there should be a limit on storage.
2. Please add information on cultural issues to the participant information, if such information is suggested as a result of Maori consultation. The Committee noted this does not need to be submitted to ethics as consultation occurs in tandem.
3. The Committee noted pharmacodynamics was being confused with pharmacogenomics (page 2 Participant Information Sheet). Please clarify whether any genetic testing was being conducted, if so this needs to be much more clearly explained and included in the consent form.
4. The Committee requested a clear explanation about what is study specific and what is standard of care, in particular with regards to human tissue. The Committee cited pages 4-6 which outlines procedures during the study, noting it was confusing, and unclear what was optional and what was mandatory.
5. The Committee query whether whole tissue block is sent – would this mean participants can’t participate in other studies? Please confirm only tissue slide(s) going.
6. The Committee queried what the certificate of consent was for, noting no procedures should occur prior to informed consent.
7. ‘Final database lock’ on Participant Information Sheet – what is this referring to?

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

1. The Committee noted that additional medicines may be required to prevent side effects from study drug. Please explain or anticipate what these medicines may be, and any further side effects from the medicines.
2. Page 17 – please change may to will cover ‘reasonable travel expenses’.
3. The Committee noted that the option to withdraw samples should be removed as the tissue has its identifiers removed - optional consent form, page 5.
4. Add information on where samples are being stored (specific within USA).
5. The Committee noted the compensation wording was out of order, in terms of the order of paragraphs. Please rearrange structure. I.e. compensation will be provided by infinity - move up to page 16, second paragraph.
6. The Committee noted that the National Ethics Committee Guidelines on Intervention Studies states that ‘If cover under the Accident Compensation Act 2001 will be excluded for the intervention study, investigators and study sponsors have responsibilities to ensure alternative compensation cover for study participants to at least ACC-equivalent standard. This may include earnings-related compensation.’ Please ensure that the Participant Information Sheet wording reflects this. Please confirm this point for the Committee.
7. Clearly explain that participants are given subject number and study code to protect their identity.
8. Remove federal legislation reference (page 18).
9. ‘This authorisation does not have an expiry date’. Page 19. Please explain more clearly what this means for example, if it refers to de-identified study data being used in the future. Be clear about identifiably and use of health information after the study, or for other studies.
10. This statement above cannot apply to tissue samples.
11. The Committee noted participants retain the right to access and correct their health information. This may result in withdrawal from study, but the participants maintain that right as study participants, as per the New Zealand Health Privacy Act and regulations.
12. Please remove yes/no options from consent form unless the statement is truly optional.
13. Pg. 21 – ‘I have agreed to store my samples for later use’ – Please remove. If banking tissue for future unspecified research please provide separate Participant Information Sheet/Consent form, in line with Ministry Guidelines on Future Unspecified Research http://www.health.govt.nz/publication/guidelines-use-human-tissue-future-unspecified-research-purposes-0
14. Page 21 – add 20 years (second to last yes no box – samples).
15. Please remove Americanisation, particularly on impacts on insurance (page 15).

Decision

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

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

This following information will be reviewed, and a final decision made on the application, by Mrs Shamim Chagani and Ms Michele Stanton.

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| **9** | **Ethics ref:** | **15/NTA/129** |
|  | Title: | “IntelliFlex™” Study |
|  | Principal Investigator: | Dr Andrew Holden |
|  | Sponsor: | Lombard Medical, Inc. |
|  | Clock Start Date: | 27 August 2015 |

Donna Katae was present in person for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The Researcher(s) stated that most of the device is currently available commercially. The Researcher(s) explained that existing aortic devices follow normal anatomy (designed to go straight down). The niche area the sponsor has identified is creating a device that can bend, or mould, around corners. First cases were beginning of 2015.
2. The Researcher(s) explained how the device works and how it is different from current devices. This device has a different, smaller, delivery system. It has a smaller hole to insert, and instead of having a dual thumbwheel and pin and pull system, the whole delivery system is a thumbwheel. This makes it more accurate. The Researcher(s) have added an exchange valve on the delivery system – half towards the back end.
3. The study is only being conducted in New Zealand.

Summary of ethical issues (resolved)

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

1. The Researcher(s) confirmed sponsor is conducting in-house monitoring. The Researcher(s) confirmed the sponsors come to hospital to monitor and access health information. The Researcher(s) confirmed the sponsor only take CRFs (de-identified data).
2. Submit letter from Dr Holden regarding the discussions around sending pre study identifiable data to the sponsor for the creation of customised grafts (note that this is current practice at the site, and that Dr Holden provides a specific information sheet to participants regarding this point – see below).
3. The Committee thanked the researchers for the peer review.
4. The Researcher(s) confirmed they are collecting demographic information and ethnicity.

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 some images are identifiable? The Researcher(s) explained that it is because devices are tailor made to the patient (in standard of care). Images of patients are sent to the company who assess images, take measurements and make the device specifically for the patient. The Committee noted that R.2.3 of the application states images would be de-identified. The Researcher(s) explained that de-identification occurs after they are enrolled into the study. The Committee noted this is appropriate.
2. The Committee asked why identifiable images are sent in standard of care. The Researcher(s) and The Committee discussed the topic. The Committee stated that the Participant Information Sheet should be clear about the identification of the images. Please explain that this is a standard of care process in the Participant Information Sheet.
3. The Committee noted that the National Ethics Committee Guidelines on Intervention Studies states that ‘If cover under the Accident Compensation Act 2001 will be excluded for the intervention study, investigators and study sponsors have responsibilities to ensure alternative compensation cover for study participants to at least ACC-equivalent standard. This may include earnings-related compensation.’ Please ensure that the Participant Information Sheet wording reflects this. The Committee noted that device studies should not reference medicine industry guidelines, as no medicine is administered.
4. On page four of the Participant Information Sheet – please clarify what is usual care for participants - ‘this is standard care following treatment’.

Decision

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

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| **10** | **Ethics ref:** | **15/NTA/130** (CLOSED) |
|  | Title: | A study of ABT-414 in combination with radiation and temozolomide, compared to radiation and temozolomide alone, in patients with newly diagnosed GBM. |
|  | Principal Investigator: | Dr David Hamilton |
|  | Sponsor: | AbbVie Pty Ltd |
|  | Clock Start Date: | 27 August 2015 |

Dr David Hamilton (CI) – Maureen Blakemore (clinical trial co-ordinator) 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.

Decision

This application was *approved* by consensus.

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| **11** | **Ethics ref:** | **15/NTA/131** |
|  | Title: | Obinutuzumab with Idasanutlin in Lymphoma |
|  | Principal Investigator: | Dr William Nigel Patton |
|  | Sponsor: | Covance |
|  | Clock Start Date: | 27 August 2015 |

Dr William Nigel Patton, Ms Carolyn Harris, a representative from Roche, 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.

Mrs Christine Crooks declared a potential conflict of interest, and the Committee decided to have Mrs Crooks stay in the room but not participate in the discussion of the application.

Summary of Study

1. The study investigates Obintuzumab with Idasanutlin. The study drug will be administered by infusion. There are 28-day treatment cycles.
2. The Committee commended the Participant Information Sheet and future unspecified research forms.

Summary of ethical issues (resolved)

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

1. The Committee asked about the ethical issues. The Researcher(s) noted that there are infusion risks, staff training risks – though being close to the hospital mitigates both of these risks.
2. The Committee queried if tumour blocks and slides go overseas, can these be returned? The Researcher(s) stated they do not send the entire block, just a slide. The Committee asked if participation in this study would preclude their participation in any other studies. The Researchers(s) stated it would not.
3. The Committee queried what procedures (eg scans) of the study are over and above usual care. The Researcher(s) stated that any study procedures are paid by the sponsor and not the DHB or participant. The Committee noted it was not an issue of who pays, but of informed consent – to know what participation involves that is different from standard of care – please include this in the PIS.

Decision

This application was *approved* by consensus.

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| **12** | **Ethics ref:** | **15/NTA/132** |
|  | Title: | The Tempo™ Study |
|  | Principal Investigator: | Prof Mark Webster |
|  | Sponsor: | Clin-Assist |
|  | Clock Start Date: | 28 August 2015 |

Mrs Jan Burd was present in person for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The study investigates a new temporary pacemaker.
2. The Researcher(s) explained that pacemakers are used to help with an electrical deficiency in the heart. Some cardiology procedures involve temporary pacemakers as standards of care. TAVI, Balloon aortic valveuloplasty and Electro physiologies (EP). Pacing is required for different reasons..
3. The Researcher(s) explained there are two issues with current temporary pacing technology – one is dislodgement (approx. 30% cases) – where the wire comes away from the surface of the inside of the heart. The sensing and measuring function is lost while it is reattached. This relates to how the pacer is fashioned to the heart. It is currently screwed into the heart wall with the hope that it stays there. The other issue is perforation (approx. 1%). This can lead to risk of bleeding into the sack around the heart, with the worst-case scenario being a rupture of the heart muscle.
4. The Researcher(s) explained product is developed by American company to address the two known risks. This design has a softer tip than the commercially available versions. The Researcher(s) stated current versions are harder, stiffer. This design is changed as it does not screw into the heart – it has two ‘capture arms’ that harness it on to the heart. The pacing lead is attached the same way – to external pace makers. This aspect is the same. It will be used during standard of care treatments. Removal is the same. Only the technology and design is different.

Summary of ethical issues (resolved)

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

1. The PIS states that a transesophageal ECHO (TEE) is sometimes done as part of standard care for one of the subgroup of patients. The result from this ECHO can make the patient ineligible for safety reasons. The use of the TEE is not included in the protocol. The researcher advised the protocol could be amended to include this as this could be a safety concern. This is a non-invasive test being performed for safety.
2. The Committee asked how long it takes to identify dislodgement. The Researcher(s) stated it is immediate. The Researcher(s) stated the dislodgement is quite common and so is actively monitored.
3. The Committee asked how long it takes to identify dislodgement. The Researcher(s) stated it is immediate. The Researcher(s) stated the dislodgement is quite common and so is actively monitored.
4. The Committee asked how conflict of interest or coercion due to investigator being treating clinician would be managed. The Researcher(s) explained that the TAVI nurse would meet patient during pre-admission visit. They will be given informed consent document and an explanation. With these procedures there are days if not weeks for patients to consider participation. Co-ordinators will approach, rather than their treating clinicians.
5. The Researcher(s) explained that tissue stays in New Zealand.

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 Researcher(s) explained how the 24 hour echo will capture any issues. The Researcher(s) confirmed that the monitoring (24 hours) is appropriate.
2. The Committee requested additional follow up as part of the protocol, beyond the current 24 hour ECHO eg a follow up clinic visit. The Committee requested 30 day follow up requirement to protocol.
3. The Researcher(s) confirmed no further follow up after 24-hour echo, provided the echo does not show any issues. The Researcher(s) added the protocol is a bit non-specific about follow up if there is an Adverse Event. It states follow up occurs until patient AE is resolved.
4. The Committee noted that the identification of exclusion resulting from echo (in TAVI cases) should be an exclusion criterion.

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

1. The Committee queried if a picture would be appropriate as the explanation was difficult to understand. The Researcher(s) explained that a prototype that can be given to the patient would be an option. The Committee noted this was a good idea – please ensure this happens.
2. The Committee noted it was potentially alarming to discuss potential perforation before it is contextualised (under risks), please review. The Committee also requested that quantification of the risks (% in application) were provided.
3. The Committee requested that the extra ECHO is made explicit – distinguish study related procedures from non-participation.
4. Page 5 – note can’t withdraw their consent for the device after the procedure, only their data from the study.
5. The Committee noted wording around removal of device should be clear regarding different types of procedures. The Researcher(s) noted there is a lot of procedural information for patients regarding their standard care (page 4). The Committee accepted this.

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*).
* Add additional follow up. The study design should be the one best suited to answer the study question, while minimising harm, maximising benefit and meeting other ethical standards. (*Ethical Guidelines for Intervention Studies para* 5.4).

This information will be reviewed, and a final decision made on the application, by Mrs Christine Crooks and Mrs Helen Walker.

## Substantial amendments

|  |  |  |
| --- | --- | --- |
| **1** | **Ethics ref:** | **14/NTA/100/AM07** |
|  | Title: | M12-963 Rheumatoid Arthritis Study |
|  | Principal Investigator: | Dr Sunil Kumar |
|  | Sponsor: | Mr Stuart Jackson |
|  | Clock Start Date: | 04 September 2015 |

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 (outstanding)

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

1. The Committee noted in the table – the 4th and 5th line listings would be considered substantial.
2. The Committee queried what action had been taken to reduce the quantity of minor deviations.

Decision

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

* Cover letter outlining what has occurred to mitigate these deviations.

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

## 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:** | 13 October 2015, 08:00 AM |
| **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 6.00pm