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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 10 February 2015 |
| **Meeting venue:** | Novotel Ellerslie |

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| **Time** | **Item of business** |
| 1.00pm | Welcome |
| 1.10pm | Confirmation of minutes of meeting of 09 December 2014 |
| 1.30pm | New applications (see over for details) |
|  | i 15/NTA/2  ii 15/NTA/4  iii 15/NTA/6  iv 15/NTA/8  v 15/NTA/9  vi 15/NTA/11  vii 15/NTA/7 |
| 4.25pm | General business:   * Noting section of agenda |
| 4.45pm | 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 | Present |
| Ms Susan Buckland | Lay (consumer/community perspectives) | 01/07/2012 | 01/07/2015 | Present |
| Ms Shamim Chagani | Non-lay (health/disability service provision) | 01/07/2012 | 01/07/2015 | Present |
| Mr Kerry Hiini | Lay (consumer/community perspectives) | 01/07/2012 | 01/07/2015 | Present |
| Ms Michele Stanton | Lay (the law) | 01/07/2012 | 01/07/2015 | Apologies |
| 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 |

## Welcome

The Chair opened the meeting at 1.11pm and welcomed Committee members, noting that apologies had been received from Ms Michele Stanton.

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 December 2014 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **15/NTA/2** |
|  | Title: | A study of Tiotropium dry powder delivered by the Monohaler device in subjects with COPD |
|  | Principal Investigator: | Dr Dean Quinn |
|  | Sponsor: | Cipla |
|  | Clock Start Date: | 29 January 2015 |

Dr Dean Quinn 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

* Dr Quinn explained that this was a phase IIA study in patients with COPD, trialling a new deviation of tiotropium dry powder through a monohaler device. He identified the key ethical issues as being people involved in the study would have to wash out of their regular medication and that blood samples will be sent overseas.
* Dr Quinn confirmed that the study would be submitted to Mesdsafe for SCOTT approval.
* Dr Quinn confirmed that this study would be testing both a generic version of tiotropium and a new device monohaler.

Summary of ethical issues (resolved)

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

* The Committee asked for clarification on the data safety monitoring arrangements. Dr Quinn advised that this would be done through the sponsor Cipla who will record changes in health or medication. This information will be reviewed by CRO monitors and medical monitors. Dr Quinn said that he is comfortable with this level of monitoring due to the dose and safety profile of the study drug, which has been in use for many years.
* Dr Quinn advised that the rescue medication will be salbutamol. Participants will need to stop their regular COPD medication 72 hours before the study visits but they will be able to use the rescue medication from six to twelve hours before the visit.
* The Committee asked if the researcher was satisfied that the peer review was sufficiently independent of the sponsor. Dr Quinn noted that he was seeking clarification on some aspects of the study design with the sponsor, for example whether participants can continue to take steroids. He agreed to pass this information on to the Committee when available.
* The Committee asked for justification on the use of placebo. Dr Quinn explained that this was so that a baseline could be provided to show what the improvement was from the two treatments.
* The Committee asked whether there were any safety concerns about patients having a wash out period and then being in the placebo group. Dr Quinn advised that participants can take rescue medication while in the unit if required. They can resume their usual medication after the 24 hour treatment period, before another wash out period 72 hours before the next treatment.
* The Committee asked whether there would be any restrictions on publication, for example if there was any safety information on the study drug (B.4.2). Dr Quinn explained that information on the drug will be published in the investigator’s brochure and this information will be made available in further trials. He thought that there was nothing to say that the information would not be published but the sponsor will determine how the manuscript is written and edited.
* Dr Quinn confirmed that only the PK samples will be sent overseas. This needs to be included in the PIS.

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

* Please remove sentence “You will be prohibited from taking below mentioned drugs during entire study period” (page 8).
* Please include the standard compensation clause from the HDEC PIS and consent form template under “what should I do if I am injured” as participants need to know that they will not be covered by ACC (page 12).
* Please remove point iv) of the consent form (page 14).

Decision

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

* Please amend the participant information and consent form, taking into account the suggestions 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 Ms Shamim Chagani and Ms Susan Buckland.

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| **2** | **Ethics ref:** | **15/NTA/4** |
|  | Title: | Investigating the effect of AIRVO on PaCO2 in patients with stable COPD |
|  | Principal Investigator: | Prof Richard Beasley |
|  | Sponsor: | Medical Research Institute of New Zealand |
|  | Clock Start Date: | 29 January 2015 |

No researchers were 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

* The Committee noted that this was a study which looked at whether the AIRVO device improved carbon dioxide levels in patients with COPD.
* The Committee commended the researcher for an application that was clearly explained.
* The Committee commended the researchers on the peer review and the rebuttal.

Summary of ethical issues (outstanding)

The main ethical issues considered by the Committee and which require addressing by the researcher were as follows.

* The Committee agreed that Fisher & Paykel would be considered the sponsor for this study (R.1.8). Please include the paragraph on commercially sponsored intervention studies (as available on the HDEC PIS and consent form template) (page 5 of the PIS) and provide evidence of sponsor insurance and CI indemnity.
* Please clarify independence of study design and operation from Fisher & Paykel.
* Please confirm whether Fisher & Paykel will place any restrictions on the publication of results.
* Please clarify how participants’ time will be reimbursed (P.3.3.1).
* Please provide more detail on how participants will be recruited through CCDHB and GP clinics.
* Please explain how participants are vulnerable (as identified in question O of the application).
* The Committee noted that there would only be a benefit to Māori if they are recruited to this study (P.4.1), how will this be addressed.

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

* Please remove the word “whether” in the sentence “Measurements of your carbon dioxide levels, heart rate and breathing rate will be used to inform whether the AIRVO for patients suffering with COPD” (page 4 of the PIS).

Decision

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

* Please amend the participant information and consent form, taking into account the suggestions by the Committee *(Ethical Guidelines for Intervention Studies, para 6.22).*
* Please provide evidence of sponsor insurance and CI indemnity *(Ethical Guidelines for Intervention Studies, para 8.4).*

This following information will be reviewed, and a final decision made on the application, by the HDEC Secretariat.

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| **3** | **Ethics ref:** | **15/NTA/6** |
|  | Title: | PINBALL Pilot RCT |
|  | Principal Investigator: | Dr Shay McGuinness |
|  | Sponsor: |  |
|  | Clock Start Date: | 29 January 2015 |

Dr Shay McGuinness 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

* Dr McGuinness explained that this is a pilot study in a group of high risk cardiac patients. He said that as standard practice, some cardiac surgery patients currently receive balloon pumps for a variety of clinical indications, before, during or after surgery. There is currently no research as to whether the insertion of a balloon pump in high risk patients before surgery reduces post-surgery complications, or other clinically relevant indicators such as inotrope use.
* Dr McGuinness explained that a previous study, 12/NTB/171, had prospectively identified patients who could be eligible for a balloon pump pre-surgery. Potential participants were then asked if they would consider taking part in a study like this. Surgeons were also asked if they would be happy to include patients in a study.

Summary of ethical issues (resolved)

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

* The Committee commended the researcher for a readable PIS.
* The Committee noted that grants had been received from the Heart Foundation and Intensive Care Foundation in Australia (submitted as evidence of peer review) and asked if any feedback had been received from the organisations, or whether the protocol had been amended as a result. Dr McGuinness confirmed that these were rigorous review process including scientific peer review, and that there was no feedback. The Committee noted that for future reference, it would be helpful to see any issues identified in a peer review that may result in changes to a study.
* The Committee asked for clarification on data safety monitoring as the protocol refers to independent experts, while R.1.4 refers to an internal data safety monitoring committee. Dr Mc Guinness explained that as the study will only run for five to six months, a DSMB would not get a chance to do any interim analysis. He said that there will only be 40 patients and as this is a regularly used intervention, the risks are known.
* The Committee asked for clarification on the risks from limb ischaemia. Dr McGuinness explained that these are high risk patients and that the operative mortality rate is around 6%; the addition of a balloon pump has minimal (if any) additional risk.
* Dr McGuinness confirmed that Māori review has been applied for but not yet received.
* The Committee asked why there would be no phase II study between this pilot study and a potential phase III study (B.1.4.1). Dr McGuinness explained that phase II studies are sometimes bypassed and that picking a composite endpoint would be difficult for this type of study.

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

* Please include that participants can withdraw from the study up until the balloon is inserted (page 3 of the PIS).
* Please clarify that participants can withdraw their data from the project at any stage (page 3 of the PIS).
* Please use compensation wording from the PIS and consent form template available on the HDEC website (page 4 of the PIS).

Decision

This application was *approved* by consensus subject to the following non-standard conditions.

* Please amend the participant information and consent form, taking into account the suggestions by the Committee *(Ethical Guidelines for Intervention Studies, para 6.22).*

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| **4** | **Ethics ref:** | **15/NTA/7** |
|  | Title: | COBALT Open Label Extension (OLE) study |
|  | Principal Investigator: | Dr Sunil Kumar |
|  | Sponsor: | AbbVie Pty Limited |
|  | Clock Start Date: | 29 January 2015 |

Dr Sunil Kumar, Mrs Catherine Howie and Ms Sandy McGreevy 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

* Dr Kumar explained that this is a phase II, open label extension, multi-centre trial of M12-963 in participants with Rheumatoid Arthritis (RA). The initial study (14/NTA/100) was for 12 weeks and participants who have done the initial part of the study will now continue treatment for a further 24 weeks.

Summary of ethical issues (resolved)

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

* The Committee asked for clarification on the recruitment issues for 14/NTA/100. Dr Kumar advised that recruitment is slow worldwide. He said as at January 15, there were 27 people randomised worldwide whereas it was expected to be approximately 60 at this stage. At his site, recruitment is on target but he is unsure of the other sites in New Zealand. Dr Kumar currently has two patients who have been randomised and are receiving treatment, with a third being randomised this week.
* Protocol for 14/NTA/100 included possible interim analysis conducted after approximately 50% subjects have at least one post baseline assessment. As recruitment is slow it will not be possible to do this prior to the two NZ patients being enrolled into the extension trial. The treatment is 12 weeks and the two NZ patients are currently at three and four weeks of treatment. The investigator confirmed they hope to enrol the first NZ patient into the extension trial in eight weeks.
* Dr Kumar advised that the six week follow up has been removed from 14/NTA/100 for those patients who volunteer to continue onto the extension study. The Committee were concerned about participants taking part in this study without safety data from the previous study being analysed.
* The Committee asked what the rationale for the extension was. Dr Kumar thought it was to further investigate the safety and efficacy of the medication. He said that it would also be beneficial for participants to continue receiving treatment rather than discontinuing treatment during the six week follow up (the Committee noted, however, that evidence of efficacy is not available until the results of Phase II are known).
* Dr Kumar confirmed that 14/NTA/100 will not be unblinded but going forward, participants will know what treatment they are receiving.
* The Committee asked why the open label extension had not been included as part of 14/NTA/100. Mrs Howie advised that the protocol had not been ready at the time of submission.
* Mrs Howie confirmed that ethical approval had not been received for any other country for the extension study at this stage.
* Mrs Howie noted that SCOTT approval has been applied for but this has not yet been received.

Summary of ethical issues (outstanding)

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

* The Committee asked for clarification on the statement that “samples may be used in comparison with the samples from people with other diseases (i.e., as controls), or to develop new diagnostics tests, research methods or technologies” (page 2 of the optional biomarker PIS). This appears to be a significant extension to the usual provisions of specified future use testing in pharmaceutical trials, and the Committee would like to see an appropriate rationale and further wording in the PIS to clearly explain this to participants.

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

* Please review the main PIS as there is currently a lot of jargon.
* Please include a sentence under reproductive risks that there is a separate PIS for pregnancy (page 7 of the main PIS).
* Please amend “samples will be stored for up to 20 years” to “data will be stored for up to 20 years” (page 10 of the main PIS).
* Please clarify whether taking back permission refers to withdrawal of consent (page 11 of the main PIS).
* Please include in the main PIS that samples will be sent overseas for testing.
* Please amend wording around withdrawal of optional samples (page 2 of the optional biomarker PIS) as this is a double withdrawal process.
* Please include where biomarker samples will be sent for testing.
* Please include whether participants will be informed of any unexpected incidental findings from the testing (points 8 and 9, page 3 of the optional biomarker PIS).
* Please include possible informational and cultural risks of taking part (page 3 of the optional biomarker PIS).
* Please include standard compensation wording from PIS and consent form template on the HDEC website (page 4 of the optional biomarker PIS).

Decision

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

* Please amend the participant information and consent form, taking into account the suggestions by the Committee *(Ethical Guidelines for Intervention Studies, para 6.22).*
* Please provide safety data from the DSMB for 14/NTA/100 to justify why this extension study should take place without evidence of safety and efficacy *(Ethical Guidelines for Intervention Studies, paras 6.47 – 6.50).*

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

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| **5** | **Ethics ref:** | **15/NTA/8** |
|  | Title: | Probenecid to boost flucloxacillin levels in clinical practice. |
|  | Principal Investigator: | Dr Jared K Green |
|  | Sponsor: |  |
|  | Clock Start Date: | 29 January 2015 |

No researchers were present for discussion of this application.

Potential conflicts of interest

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

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

Summary of ethical issues (outstanding)

The main ethical issues considered by the Committee and which require addressing by the researcher were as follows.

* The Committee noted that this study has been identified as an observational study but it is not clear whether the three dose regime being tested is standard practice. Please clarify whether the dosing is a standard practice in which case it will be an observational study or whether it is not standard care in which case it would be an intervention study.
* Please clarify if samples will be sent overseas for testing and if so, please include this in the PIS.
* The Committee noted that participants may find it difficult to say that they feel uncomfortable discussing the study with their treating physician and recommended that the treating physician does not take part in the invitation and discussions of the study.
* Please provide comment on Dr Tim Blackmore’s peer review and whether this will result in any changes to the protocol or participant information sheet.

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

* Please include in the consent form that blood samples will be taken.
* Please either include the risks associated with pregnancy (identified in the consent form) in the PIS, or remove the statement in the consent form (given this is an observational study it would appear not to be necessary.
* Please remove yes or no boxes on the consent form for statements that are not truly optional.

Decision

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

* Please confirm whether the dosing regime is currently standard practice *(Ethical Guidelines for Observational Studies, para 2.2).*
* Please amend the participant information and consent form, taking into account the suggestions by the Committee *(Ethical Guidelines for Observational Studies, para 6.10).*

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

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| **6** | **Ethics ref:** | **15/NTA/9** |
|  | Title: | Metformin 500 mg bioequivalence study conducted under fed conditions |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Generic Partners Pty Ltd |
|  | Clock Start Date: | 29 January 2015 |

Dr Noelyn Hung, Dr Tak Hung and Mrs Linda Folland 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

* Dr Noelyn Hung explained that this study will compare the absorption of 500mg metformin in healthy volunteers under fed conditions. A previous study has tested doses of 1,000mg under the same conditions.

Summary of ethical issues (resolved)

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

* The Committee commended the researchers for the detailed peer review.
* The Committee asked if Generic partners was GMP certified. Dr Tak Hung advised that Generic partners is a virtual company that will contract manufacturers to make pharmaceuticals such as the metformin bioequivalent. He confirmed that GMP certification is required to meet e FDA, EU and TGA regulatory requirements. Mrs Folland confirmed that they have the GMP certificate for the product being used in this current clinical trial which is needed for Medsafe approval.

Decision

This application was *approved* by consensus.

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| **7** | **Ethics ref:** | **15/NTA/11** |
|  | Title: | Stroke navigator development study |
|  | Principal Investigator: | Dr Dianne E Roy |
|  | Sponsor: |  |
|  | Clock Start Date: | 29 January 2015 |

Dr Dianne Roy and Professor Gillian Whalley 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

* Dr Roy explained that there are many navigator services available but there is not a lot of evidence to show what is likely to work. Professor Whalley noted that this is a navigator for families which is not currently a DHB service.

Summary of ethical issues (resolved)

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

* The Committee noted that this study could have been conceptualised as a service evaluation or as an intervention. This was discussed with the researchers, including the different ethical aspects of these study designs. Framed as a service evaluation it would have been considered low risk observational research. The researchers will consider whether they wish to reframe their application; however they have proceeded with the stroke navigator role as an intervention (development of the role in a new disease group, not cancer), and wish to determine as far as possible whether this is an effective intervention.
* The Committee noted that the comparator group at North Shore would get usual care and they asked if the researchers thought this was a fair comparator group. Professor Whalley advised that there will be demographic differences between the two groups (North Shore and Waitakere) but that contamination cluster randomised approach seemed the most statistically valid way to provide evidence of effectiveness.
* Dr Roy explained that there will be six patients and their whanau recruited at each of the sites. She said that one of the inclusion criteria was a stroke survivor with at least two family members. This would mean there would be a minimum of 36 participants but it could be up to 50 or 60 as participants would not be excluded if there were more than two family members.
* Dr Roy confirmed that the stroke survivor would complete the quality of life and functional independence measures questionnaires and the family would complete the quality of life and modified caregiver strain index questionnaire. Therefore separate PIS are required for the stroke survivor and another for the family member (s), with the different procedures for each clearly outlined (including the patient healthcare utilisation for the patient PIS).
* As this is a feasibility study, the researchers agreed to exclude participants who are unable to give informed consent due to cognitive impairment. This will be added to the exclusion criteria and a record of how many stroke survivors who were not competent to give consent will be kept.
* The Committee asked what consultation had been undertaken with Māori for the study design. Dr Roy explained that they have worked with Māori advisors throughout the study design, along with having focus groups with Māori advisors from Waitemata DHB Unitec in developing the stroke navigator job description. She said that the study is currently with Dr Helen Wihongi for formal review.
* Professor Whalley advised that they want to include a Māori and a non- Māori stroke navigator and they are currently developing a job description for this. The Committee asked if there would also be Māori researcher conducting the interviews. Dr Roy confirmed that there would be.
* The Committee asked why the data generated had been listed as potentially identifiable (R.2.4). Dr Roy confirmed that while the data would be kept confidential, with small samples of qualitative data, there is always the small risk that an individual could be identified by somebody that knew they were taking part in the study.
* The Committee asked if the stroke navigator service would only be provided for the health of older people service or would any stroke patients across the hospital have access to it. Dr Roy confirmed that the stroke navigator would be available across all services. This was particularly important, given that Māori tend to have strokes at a younger age.

Summary of ethical issues (outstanding)

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

* Please provide copies of all questionnaires and semi structured interview questions that will be used.
* Please clarify whether the comparator group will be consenting participants.

Please clarify whether the patient participant needs to consent to their family also being participants.

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

* Please provide a separate participant information sheet and consent form for family members.
* Please include in the PIS what data will be collected during data collection and follow up and what will be done with this data.
* Please include in the consent form whether a participant’s health professional or GP will be told that they are taking part in the study.

Decision

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

* Please amend the participant information and consent form, taking into account the suggestions by the Committee *(Ethical Guidelines for Intervention Studies, para 6.22).*
* Please provide a separate participant information and consent form for family members *(Ethical Guidelines for Intervention Studies, para 6.22).*
* Please provide copies of the questionnaires and interview questions.

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

## General business

1. The Committee noted the content of the “noting section” of the agenda.
2. The Committee agreed to send any comments on the NEAC cross-sectoral ethics arrangements for health and disability research discussion document to the Chair.
3. The Committee agreed to include the table on appropriate forms of data monitoring (page 30 of the *NEAC Ethical Guidelines for Intervention Studies*) in future agendas.
4. The Committee agreed that it would be helpful to have the Chair of SCOTT come and speak at a future HDEC meeting. Areas of discussion that would be useful include the SCOTT process, GMP certification, peer review and their thoughts on the testing of generic drugs.
5. The Chair reminded the Committee of the date and time of its next scheduled meeting, namely:

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| **Meeting date:** | 10 March 2015, 08:00 AM |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

The following members tendered apologies for this meeting.

* Mr Kerry Hiini

The meeting closed at 4.40pm.