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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 11 August 2015 |
| **Meeting venue:** | Novotel Ellerslie |

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| **Time** | **Item of business** |
| 1.00pm | Welcome |
| 1.00pm | Confirmation of minutes of meeting of 14 July 2015 |
|  | New applications (see over for details) |
| 1.30pm | i 15/NTA/93  ii 15/NTA/97  iii 15/NTA/98  iv 15/NTA/101  v 15/NTA/102  vi 15/NTA/103  vii 15/NTA/104  viii 15/NTA/105  ix 15/NTA/106  x 15/NTA/107  xi 15/NTA/108 |
| 6.30pm | 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 | Present |
| Ms Susan Buckland | Lay (consumer/community perspectives) | 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 | 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 (intervention studies) | 01/07/2013 | 01/07/2015 | Present |

## Welcome

The Chair opened the meeting at 1.05pm and welcomed Committee members.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

The Committee welcomed Mrs Fox Swindells, a new HDEC advisor.

## Confirmation of previous minutes

The minutes of the meeting of 14 July 2015 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **15/NTA/93** |
|  | Title: | LAAOS 3 |
|  | Principal Investigator: | Dr Shay McGuinness |
|  | Sponsor: |  |
|  | Clock Start Date: | 23 July 2015 |

Dr Shay McGuinness was present by teleconference for 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 multi-national study, based in Canada.
2. The study procedure aims to treat atrial fibrillation (AF).
3. The Researcher(s) explained that there is clinical uncertainty about the usefulness of appendage closure procedure, used to remove the left atrial appendage (study intervention). This study will answer if it is a beneficial procedure or not.
4. The Researcher(s) confirmed a pilot study in Canada, as well as single center studies, has generated some evidence that has informed this study
5. This study involves 5000 patients internationally (300 NZ).
6. Funded by Canadian Institute of Health Research and National Medical and Health Research Council in Australia. Funding will be sought from the Health Research Council in New Zealand.
7. This is the largest intervention study ever conducted on cardiac patients undergoing surgery.

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 whether there are any risks involved in conducting the procedure. The Researcher(s) stated that the participants are those with history of AF who are having cardiac surgery as their standard of care. We are not recruiting anyone who would not be undergoing surgery. To conduct the procedure it takes less than 10 minutes and there are various methods to do it. The most common is to use a vascular stapler, a standard plastic surgery tool. This is used to cut off the appendage. The main risk is to add 10 minutes to surgery. The average length of surgery is 4-5 hours, so it does not lengthen the surgery very much. By removing the tissue it creates a very minor risk of bleeding, however it is a low-pressure part of the heart.
2. The Committee noted the Participant Information Sheet cites a 15% risk of bleeding. The Researcher(s) stated this is at the extreme end.
3. The Committee queried how often the study procedure actually occurs in New Zealand. The Researcher(s) stated in Auckland there are 7 surgeons. 1 surgeon would do it in almost every patient, 1 1/3 of the time, 1 a bit less than this and the others do not perform it. The Committee suggested adding this to Participant Information Sheet as it contextualizes the use in New Zealand and shows the clinical uncertainty.
4. The Researcher(s) confirmed study is investigator led.
5. MPS expired in January – please resubmit via email to [HDECS@moh.govt.nz](mailto:HDECS@moh.govt.nz)

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

1. Page 2 – Potential Risk – ‘this procedure’ – clarify that it is the appendage closure.
2. ACC – the institution changed its name – please amend / update.
3. Page 2 – risk of stroke from AF is 4% a year – please move this to the starting paragraphs. This is not a risk of the actual study procedure.
4. Add length of storage of health information (15 years in application).
5. Add that the GP will be notifed in Participant Information Sheet text. The Committee notes it is in the consent form.
6. Add more information on the actual procedure including more information on why it is being performed. The Committee suggests a picture.
7. Add information on the local processes for disposal or return of tissue, which will be particularly relevant for Maori.
8. Explain under withdrawal, once procedure is done it is irreversible – for clarity.
9. Add that it is largest cardiac trial ever conducted.

Decision

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

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| **2** | **Ethics ref:** | **15/NTA/97** |
|  | Title: | CEDAR: Safety and Efficacy of Abicipar Pegol (AGN-150998) in Patients With Neovascular Age-related Macular Degeneration |
|  | Principal Investigator: | Prof Philip Polkinghorne |
|  | Sponsor: | Allergan Inc. |
|  | Clock Start Date: | 30 July 2015 |

Philip Polkinghorne (Co-investigator) and May Mendoza 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. Macular Degeneration is the number one cause of blindness in New Zealand and in the world.
2. The Researcher(s) explained that the study drug might reduce the number of injections required to treat the disease. The estimate is a reduction from monthly visits to 3-4 monthly.
3. The Researcher(s) explained that there was a very similar study that has had 13 New Zealand participants. This involved treatment with the study drug for 3 months and has a long-term follow up period. The earlier study compared against gold standard treatment. This current application involves one year of treatment with the study drug.

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 they are looking for non-inferiority, or the same treatment effect as standard treatment, with fewer injections.
2. The Researcher(s) confirmed 2 out of 3 chance of getting active study drug in this trial.
3. The Researcher(s) explained the sham procedure. The Committee queried whether the study is blinded. The Researcher(s) explained that there are two investigators, one is blinded (assessing investigator) but one won’t be, in order to administer the injections.

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 withdrawing in writing is not required. Participants can withdraw verbally.
2. The Researcher(s) explained that the tissue samples and photos were ‘owned’ by the sponsor. The Committee noted that it was unclear what happened with human tissue, and participants are usually given the ability to withdraw their samples unless they have been delinked. Please clarify the withdrawal rights in relation to samples. This needed significant clarification by the sponsor and in cases where there was future use of tissue there would need to be further Participant Information Sheets (the application currently states that there is no future unspecified use b.4.5; please confirm). Please see the Ministry of Health Future Unspecified Research Guidelines for guidance <http://www.health.govt.nz/publication/guidelines-use-human-tissue-future-unspecified-research-purposes-0> .
3. The Committee queried if, once study is over, participants have access to best available treatment? The Researcher(s) explained that it depends on approval of the drug. The participant can either be referred to public system or they can continue with the drug privately.
4. The Committee queried about the ‘escape to standard treatment’ paragraph in the Participant Information Sheet. The Researcher(s) explained that if a participant wanted to leave the study they would revert their care to standard care. This may be because they have an adverse event, or did not respond well to the study drug.
5. The Committee clarified that this is a situation that occurs if someone meets the list of reasons for study removal in the protocol. The Researcher(s) confirmed that this was correct. The Committee requested this is made clearer in the Participant Information Sheet.
6. The Committee queried why Maori consultation was stated as not required? The Committee requested that consultation occurs. Please view Health Research Guidelines for Research Involving Maori for guidance.
7. The Committee queried whether participants would be patients from the researcher’s own clinic. The Researcher(s) explained it would be a mixture – some participants from universities, some will be our own patients and some from public and private optometry practices. The Committee requested an explanation about how conflict of interest will be managed. The Researcher(s) explained that when we they see a patient that is potentially eligible they tell them about the study as well as standard of care options. The Researcher(s) explained that there is always potential for coercion however they have a clinical management committee that monitors our treatments.

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

1. Remove ‘race’ from page 2 of the PK optional testing Participant Information Sheet. Ethnicity is the preferred term.
2. Explain what PK testing is, where samples are stored, how long they are kept.
3. Add OPTIONAL to the PK testing Participant Information Sheet.
4. The Researcher(s) stated they would use the term ‘study eye’ in the Participant Information Sheet.
5. Clearly explain that only one eye receives the experimental drug, in cases of bilateral involvement of disease.
6. Page 16 – please include in the paragraph about data being sent offshore that it is coded data.
7. Please clarify in consent form – photograph taken of me to photograph taken of my eye(s).
8. Add separate contact details for Maori support.
9. Please include that the drug is not yet approved.

Decision

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

* The researchers are required to carry out Maori consultation as per the Health Research Council Guidelines for Research involving Maori.
* Please address how the study may benefit Māori and how cultural issues that may arise for Māori participants in the study will be managed (*Ethical Guidelines for Intervention Studies* *para 4.7*).
* 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*).
* Explain how the conflict of interest resulting from care provider being the researcher is addressed *(Ethical Guidelines for Intervention Studies para 4.19)*

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

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| **3** | **Ethics ref:** | **15/NTA/98** |
|  | Title: | PINTO |
|  | Principal Investigator: | DR Ruth Hughes |
|  | Sponsor: |  |
|  | Clock Start Date: | 30 July 2015 |

Ruth Hughes 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 Researcher(s) explained that the study is a feasibility study that will inform a larger trial to compare Ministry of Health national guidelines against local practices.
2. The Researcher(s) noted that Ministry guidelines recommend that HbA1c is added to first set of antenatal bloods for all women in New Zealand, to identify potential pre-existing diabetes. 41-49 mmol is the pre-diabetes range. If a high result is identified the women receive usual dietary and exercise advice with their Lead Maternity Carer (LMC). The guidelines acknowledge that other centers in New Zealand treat these women as if they have gestational diabetes.
3. The Researcher(s) stated their study caps the pre-diabetic range at 46 mmol. New Zealand is different to international cutoff (48 mmol internationally - 50 mmol and above in New Zealand). This is based on their recent research which found significant maternal and infant outcome difference above 46 mmol.
4. The Study randomises between treating pre-diabetic women as if women have gestational diabetes (with intensive early intervention) and the current Ministry guidelines (standard of care).

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 women with higher levels are known to have very increased risks during pregnancy. The Researcher(s) did not feel comfortable randomising up to 50 mmol – and therefore exclude these women and will treat them as if they had gestational diabetes. This reduces risk involved with randomisation.
2. The Committee queried if the Ministry of Health or the investigators initiated study. The Researcher(s) explained it was the researchers, clarifying they were not approached by the Ministry however the Ministry had acknowledged the information gap in the current guidelines.
3. The Committee noted this is a feasibility study. The Researcher(s) confirmed it was, explaining they need this study to determine how to measure pregnancy outcomes. The Researcher(s) need to recruit at very early pregnancy – much of the risk factors develop early as the placenta is fully formed by 16 weeks. The negative outcomes that they are interested in are related to the placentation process. There are ‘classic risks’ from diabetes, such as large babies, but these are more related to control of blood glucose in second half of pregnancy. Theoretically both groups would receive treatment in second half of pregnancy. This study aims to see whether this early intervention will result in any outcome changes.
4. The Researcher(s) explained that the study also aims to identify how many women would be needed for a full study – to determine what outcomes will be most useful. Other feasibility endpoints include sustainable recruitment rates and intervention compliance. For the full study they may also look at on-going long term childhood outcomes.
5. The Researcher(s) confirmed only birth data for the infant is collected for this feasibility study. No childhood data will be collected.
6. The Committee queried what study information becomes health information for the participant? The Researcher(s) explained that most if not all of it would become health information, adding most data is collected as part of standard care. This data is collected from lead maternity care (LMC) providers and delivery hospital records. The Researcher(s) confirmed this data would go into case report forms.
7. The Researcher(s) confirmed they took on the Health Research Council reviewer comments. The Researcher(s) explained the harm prevention comment was mitigated by their usual care practices. Regarding the outcomes comment – The Researcher(s) specified the proposed outcomes after the comments, though we can’t be 100% as this feasibility study aims to refine the outcome data points.
8. Regarding the resources to achievement of appropriate ethnic-specific recruitment given the burden of disease in Maori and Pacific populations – the Researcher(s) are recruiting midwifery staff so there is no significant resource impact. There are specific LMCs in Christchurch who will see large amount of Maori and Pacific Island women, they will ensure that these LMCs will be trained and involved.
9. The Committee noted Maori and Pacific systematically book later in pregnancy, which means the researcher might miss the most important and vulnerable patient population (in relation to diabetes). The Researcher(s) explained that education initiatives are helping mitigate this but acknowledged that it was difficult to ensure they captured Maori and Pacific island women.
10. The Committee suggested getting a GP involved as most women in Auckland see a GP about pregnancy prior to them being potentially recruit able for the study (booking in with midwife etc.).
11. The Committee noted it was important to know if non-responders were the same as responders. The Committee noted this could be drawn from audit. Data can used if it is de-identified, and therefore did not require the consent to include birth data even if not consenting to the main study. It was also noted that if women did not give consent to use of their de-identified data then this could mean that the researcher could not confirm whether their sample was a valid representation of birthing women (impact on study validity).
12. The Committee queried how those women with diabetes would ensure adequate care in the DHB diabetic clinic setting due to resourcing directed to the study, and for any earlier intervention procedures. The Researcher(s) noted there are group sessions twice a week. This involves a dietician – this is standard care, not study specific. It will include diet and exercise plans. During these sessions their research midwife will come and talk about the study.
13. The Committee queried whether there will be any formal data safety monitoring for the feasibility? The Researcher(s) stated HRC advised it was not required. The Committee noted the intervention is not harmful.
14. The Committee requested clarification on the Christchurch women (optional blood test). The Researcher(s) explained that this related to tests to look at developing complications at the 20-24 week mark, based on previous research. There is no data to suggest whether diabetes played a role in this work so they saw this as an opportunity to collect this tissue. The Committee noted this should be explained in the Participant Information Sheet. Make it clear that results will not be communicated back to women as a clinical finding. The PISCF says blood samples will be destroyed a few days after collection while the application r.3.7 says the blood samples will be stored in a freezer. Please clarify and correct the PISCF. If the samples are stored then further information will be required, particularly if they are to be kept for future unspecified use http://www.health.govt.nz/publication/guidelines-use-human-tissue-future-unspecified-research-purposes-0.

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

1. Take out top of page 7 – not required for feasibility.
2. The Committee noted that if any unexpected clinical findings are identified via the questionnaire, such as depression, these must be followed up – add to Participant Information Sheet.

Decision

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

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| **4** | **Ethics ref:** | **15/NTA/101** |
|  | Title: | FILLY |
|  | Principal Investigator: | Prof Philip Polkinghorne |
|  | Sponsor: | CNS - Clinical Network Services Ltd. |
|  | Clock Start Date: | 30 July 2015 |

Philip Polkinghorne (CI) and May Mendoza was present 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 there is a 1 in 7 chance in having macular degeneration at the age of 50, and 1 in 3 chance at the age of 80.

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 why the pregnancy information was so substantive given the age range of the potential participants. The Committee accepted the rationale.

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 trial must be registered with a clinical trial registry.
2. The Committee queried why Maori consultation was stated as not required? The Committee requested that consultation occurs. Please view Health Research Guidelines for Research Involving Maori for guidance.
3. The Researcher(s) explained that the tissue samples were ‘owned’ by the sponsor. The Committee noted that it was unclear what happened with human tissue. This needed significant clarification by the sponsor and in cases where there was future use of tissue there would need to be further Participant Information Sheets. Please see the Ministry of Health Future Unspecified Research Guidelines for guidance.
4. The Committee asked why blood tests are taken. The Researcher(s) explained they would conduct genetic analysis to look at phenotypes to determine if and why some patients respond better than others. The Researcher(s) explained that in standard of care therapy there is variance of effectiveness. The Researcher(s) suspect there are subgroups of people who have different reactions to treatments, or different classes of drugs. The Committee noted more information was needed in the PISCF on this point.
5. The Researcher(s) confirmed the restrictions on publishing are standard.
6. The Committee noted there are a number of requirements to include about what happens to human tissue. This includes information on pharmacogenomics use. The Committee noted that samples are destroyed (in application) but requests that the sponsor clarifies this information Please confirm whether tissue will be stored for future research.
7. The Committee queried whether it was possible for sham participants to access treatment arm, if it is proven to be a good intervention, after the study. The Researcher(s) stated it depended on study drug approval and funding. The Researcher(s) estimated it would take some time to analyse the study results, adding that being in the sham arm would not preclude anyone from having access – but stated there is no current plan to provide study drug post study. Standard of care would be provided, but this would not involve study drug.
8. The Researcher(s) stated at present time there is no current treatment for dry macular degeneration. The Committee stated that is more reason to ask the sponsor to provide continued access after the study. Please explain after sponsor has been consulted. This is not a requirement – rather a clarification.

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

1. The Committee noted that the consent form has many tick boxes that are not truly optional. Only retain those that are optional and make those that are not optional a statement.
2. Please include that the drug is not yet approved.
3. Page 14, second paragraph, remove second sentence ‘you also agree to allow the study doctor and…store and perform any tests.’ This appears to be allowing blanket consent to performing tests and in inappropriate.
4. Page 2 – change which HDEC is referred to.
5. Please explain terminology or reference where definitions can be found (page 5).
6. Explain what laboratory tests are and or for (page 5).
7. Please consult MOH guidelines and ensure the PIS complies with these requirements.

Decision

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

* The researchers are required to carry out Maori consultation as per the Health Research Council Guidelines for Research involving Maori.
* Please address how the study may benefit Māori and how cultural issues that may arise for Māori participants in the study will be managed (*Ethical Guidelines for Intervention Studies* *para 4.7*).
* 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*).
* **If required due to storage of tissue beyond the study:** Please provide a separate Participant Information Sheet and Consent Form for the use of tissue for future unspecified research (*Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes, para 2*).
* Explain how the conflict of interest resulting from care provider being the researcher is addressed *(Ethical Guidelines for Intervention Studies para 4.19)*

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

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| **5** | **Ethics ref:** | **15/NTA/102** |
|  | Title: | Study to Assess the Efficacy and Safety of PT010 Relative to PT003 and PT009 on COPD Exacerbations in Subjects With Moderate to Very Severe COPD |
|  | Principal Investigator: | Dr Dean Quinn |
|  | Sponsor: | inVentiv Health Clinical Australia Pty Limited |
|  | Clock Start Date: | 30 July 2015 |

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

1. The Researcher(s) explained that this company uses new technology to administer drugs. This is the 6th study that CI has participated in with the sponsor. The technology allows combination medications to be used within the same inhaler. The technology also allows no drug-drug interaction, as they are separate in the platform that delivers the drug.
2. The Researcher(s) stated the study aims to reduce exacerbation of COPD.
3. The Researcher(s) stated there are 4 arms of the study. Each arm has a different method of treatment.

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 sub-studies. The Researcher(s) explained they are additional studies. The Committee noted they are low risk, do not involve storing human tissue and non-invasive.
2. The Researcher(s) acknowledged that there is no need to provide written withdrawal of consent. The Committee noted that it is useful to have a flag if someone wants to withdraw and there is safety follow up that is required or appropriate. The Researcher(s) agreed.
3. The Committee asked about the restrictions on publication. The Researcher(s) explained this sponsor is very accommodating with their publication processes.
4. The Committee noted there is an ethical obligation to publish study results, even when results are negative.
5. The Researcher(s) noted the study drugs are often considered better than on the market drugs. This relates to efficacy of medication as well as the delivery mechanisms. In terms of recruitment it is about reviewing what each participant is eligible for and their level of COPD and what drugs are funded.
6. The Committee queried how Maori and Pacific would be target to ensure they benefit from the study given the substantial burden of disease in these populations. The Researcher(s) stated their database has many Maori and Pacific Island people who will be approached to participate. We will also recruit from the community, and are consulting with Maori research groups – this is ongoing due to past studies.

Summary of ethical issues (outstanding)

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

1. Please make it clear when health information will be destroyed – confirm with sponsor and respond to HDEC in a cover letter.

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

1. The Committee noted the Participant Information Sheet was very long and complicated. The Researcher(s) agreed. The Committee noted there is a lot of repetition and suggested that a table would be useful in covering multiple procedures. Time, events etc. Please reduce length and explain what has been changed in a cover letter.
2. The Committee suggested condensing study visits, ‘same as visit 1 except added X’.
3. The Committee noted Americanization of Participant Information Sheet. Please revise.
4. The Committee noted Participant Information Sheet could be more gently worded.
5. The Researcher(s) explained people could withdraw with various levels of remaining engagement with researchers in the ‘vital status’ section. Please clear what is being asked of participants and why; currently this is confusing.
6. Page 2 asks for participants to provide a reason for leaving study. Note that there is no need to give a reason. Please make this clear to participants.
7. Page 8 – The Committee queried what blood tests are for regarding the spirometer tests. The Committee requested this is clarified both for the Committee in a cover letter and in the Participant Information Sheet for participants.
8. Page 3 – change ‘race’ to ethnicity.
9. Make it clear how much time there is between the study screening visits.
10. Remove mention of stopping trial for commercial reasons.

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*).
* Explain what happens to health information (*Ethical Guidelines for Intervention Studies* *para 7.7)*

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

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| **6** | **Ethics ref:** | **15/NTA/103** |
|  | Title: | GS-US-223-1018: Study Evaluating GS-4997 Pharmacokinetics in Subjects with Normal and Impaired Hepatic Function |
|  | Principal Investigator: | Prof Edward Gane |
|  | Sponsor: | Gilead Sciences, Australia New Zealand |
|  | Clock Start Date: | 30 July 2015 |

Carolyn Harris (study co-ordinator) and Paul Hamilton were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This is a phase I efficacy and safety study.

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 a non-therapeutic study is being used in a group that is not the patient population the drug is intended for.
2. The Committee queried why patient population was participants with liver disease rather than diabetes, noting that the Participant Information Sheet talked about the potential value of the study drug for people with diabetes. This is likely to be confusing for participants and requires further explanation to the Committee and potential participants. The Researcher(s) noted it was phase I study in participants with hepatic impairment. These participants are chosen because they have trouble processing drugs. The study drug has been shown to have a hepatic metabolism – it could therefore result in a slower or delayed metabolisation of the drug. The Researcher(s) added there could be a degree of liver impairment in other patient populations due to expected comorbidities – so this study will try and determine what a therapeutic dose would be in cases where there are liver impairments.
3. The Researcher(s) explained the drug has been tested in a few phase I healthy volunteer studies (400 people internationally), with some phase I and phase II studies in other patient populations.
4. The Researcher(s) explained they were seeing more co-morbidities so it was important to know how dosing would work in those with impaired liver function, as well as eventually testing in diabetes participants too.
5. The Committee queried the PIS comment about participants not accessing health information during the study. The Committee noted under the Health Information Privacy Code participants always have the right to access and correct their study data – though this may mean they will be withdrawn from the study. The Committee also requested that ‘after the study is over’ is clarified – is this the single dose, or 15 years?
6. The Committee noted participants do not need to withdraw from the study in writing. Please remove this.
7. The Researcher(s) clarified participants are inpatients for 6 days.
8. The Committee queried how participants are recruited. The Researcher(s) explained that various hospitals around New Zealand would provide referrals. These participants will indicate they want to be contacted.
9. The Committee queried data safety monitoring – how will you ensure participants are safe? The Researcher(s) explained inclusion criteria require stable participants, not involving anyone with health problems or many hospital visits or changes in their medications. While they may have severe liver disease it will be stable liver disease. They will have blood tests with a full range of monitoring plans. These assessments are built into the study protocol. The Researcher(s) confirmed they do not anticipate any long term effects, citing the half life of the study drug.
10. The Committee queried the potential for damage to liver, citing animal studies. The Researcher(s) stated no expectation to liver function.

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 all samples and study data is sent to the sponsor in a de-identified form. Data is stored for future analysis. The Committee requested a timeframe for this storage.

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

1. The Committee requested that the acronym PK is expanded and then refer to where it is explained.
2. Add notification of GP as mandatory to participate.
3. Please revise the Participant Information Sheet and explain this to participants, in lay language. i.e. this drug could be good for diabetics but we need to test it in people with bad livers to see how it works when it can’t be processed very well.
4. Remove reference to ‘state law’ page 4.
5. Add information about where tissue is going overseas and importance of tissue for Maori.
6. Please amend ACC reference – please use HDEC template. Please remove clause ‘harm is unlikely’, noting this is a phase I trial.

Decision

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

* Clarify whether the need to conduct hepatic studies is related to FDA requirements – if it is not please clearly explain rationale to HDEC.
* 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*).
* Explain what happens to health information (*Ethical Guidelines for Intervention Studies* *para 7.7)*

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

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| **7** | **Ethics ref:** | **15/NTA/104** |
|  | Title: | Glucose in Well Babies (GLOW) |
|  | Principal Investigator: | Dr Deborah Harris |
|  | Sponsor: | Waikato District Health Board |
|  | Clock Start Date: | 30 July 2015 |

Dr Deborah Harris 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 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 determining the glucose and ketones in newborns is important because there is a gap in knowledge about ‘normal levels’, only a focus on low glucose – for example low glucose could actually be quite common in newborns and not a medical problem.
2. The Researcher(s) explained that diagnosis and treatment of low blood sugar in newborns was her PhD topic. The Researcher(s) had also led a prior study involved assessing a non-invasive gel to increase blood sugar for high-risk babies.
3. The Researcher(s) has spent time studying ketones and lactates and how these are used as energy for the brain of newborns. They have developed ways to measure these in small amounts of blood.
4. The Researcher(s) stated newborns might be over-treated in regard to glucose, and therefore the impact of this research might be rethinking low glucose management guidelines.
5. The Committee requested comment on invasiveness of tests. The Researcher(s) stated heel pricks are required to answer the study question. Some babies feel it and some babies sleep through it. There are studies that show that if you conduct the heel pricks during feeding it results in less distress or pain. With continuous glucose monitor – The Researcher(s) has inserted over 700 of these with no problems. The sensor is fine as a piece of hair. There is always a risk of infection but this comes with all procedures. Babies can bath with them in. Other studies have had them in for 7-14 days. In this study the sensor will be left in for 5 days. The Researcher(s) explained that this is due to the relationship to breast milk coming in on day 4. The hypothesis is that babies have low blood sugar until feeding occurs.
6. The Committee queried if there is expectation to breastfeed? The Researcher(s) stated no, they want to follow what is natural and normal – so if some want to breast feed or formula feed, they will capture all of this data. This will provide interesting evidence in its own right.
7. The Committee queried if data will be individually fed back to participants or as a full study result? The Researcher(s) stated full study result – the researcher will be blinded until the end of the study.
8. The Committee queried how participants were recruited? The Researcher(s) stated midwifery clinics in Waikato area. The Researcher(s) has spoken to many midwives and they seem to be very enthusiastic. It is important for the mothers to be healthy too. Health monitoring of mothers is part of normal antenatal care.
9. The Committee queried when the researcher would engage with potential participants. The Researcher(s) stated that the midwives would contact the researcher and then the researcher makes engagements pre-delivery, in order to have time to consider participation. The Researcher(s) plans to speak with both family members and wider family if appropriate, and will have more than one opportunity to talk about participation.
10. The Researcher(s) noted that continued support due to study participation was reassuring for participants in her community consultation to date.
11. The Researcher(s) confirmed that consent occurs then there are eligibility criteria and exclusion criteria that come into effect after birth.
12. The Committee queried who will provide consent – would it always the mother? The Researcher(s) stated yes, primarily the mother but could be both parents.
13. The Researcher(s) stated that they have strong relationship with Maori research group at Waikato.
14. The Researcher(s) stated if baby becomes unwell for any reason at all they would go down usual clinical channels for an unwell baby. It is unlikely but certainly possible. At this point they would receive whatever treatment they needed. From the point of view of the study the researcher will not know anything additional to standard care testing.
15. The Researcher(s) clarified tissue tests are point of care, no storage of blood samples including the umbilical sample.
16. The Committee queried the sample size calculations due to the invasiveness of the test and the vulnerability of the study population (ethical imperative to conduct in the smallest possible sample to provide valid results). Jane Howden, a UK researcher, has shown that low blood sugars happen 14-15% of the time in normal term babies. A power calculation was based on this. The variation and range of glucose concentrations also assisted in the power calculation of the study. They looked at prior studies and the range and distribution – a statistician helped them identify a 0.1 level of precision needed at least 50 babies. They have allowed for a drop out 25% withdrawal. The Researcher(s) confirmed they could stop recruitment at successful recruitment of 50 participants.
17. The Committee queried exclusion criteria of a BMI over 30. Will this systematically exclude some ethnicities, such as Pacific women? The Researcher(s) acknowledged that higher BMI result in different glucose levels for babies. The Researcher(s) cited literature. The Committee queried if there will be any additional recruitment strategies to achieve appropriate representation of Maori and Pacific participants within the BMI cutoff limit.

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

1. The Committee requested the ACC wording used from HDEC template is added.
2. Add HDEC contact details. See HDEC template for guidance.
3. Add Maori support contact details.
4. Add statement that the glucose monitor will be attached for 5 days.
5. Noted age of majority is 20 in New Zealand. Please store health information for 10 years after 16.
6. Add some further information on patient rights – right to access and correct their data. Explain that doing so before the trial is complete may result in withdrawal from the study, as the study is blinded – but the right to do so remains.

Decision

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

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| **8** | **Ethics ref:** | **15/NTA/105** |
|  | Title: | Tiotropium inhalation powder bioavailability study |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Cipla Limited |
|  | Clock Start Date: | 30 July 2015 |

Noelyn Hung (CI), Linda Folland (administration manager) and Tak Hung (co-investigator) will 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 Committee queried why the study was closed. The Researcher(s) explained that the sponsor is citing commercial sensitive due to their dosing plan.

Summary of ethical issues (resolved)

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

1. The Committee requested that page 16 of application – ACC equivalent must be met.

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 hepatitis is notifiable under the Health Act 1956. Management of positive results was discussed. Please note in the Participant Information Sheet that a positive hepatitis test will be notified to the relevant health authorities.
2. The Researcher(s) stated they would inform the GP who would further diagnose. The Committee requested that this is made clear.
3. Make it clear that legal and cultural advice is prior to participation.
4. Please ensure international students know what they are getting themselves into and that they have either a GP or contact with student health.
5. Were there any adverse events in previous studies? The Researcher(s) stated there were none.
6. Please use ethnicity collection method that is in line with Ministry of Health census 2001 questions https://www.**health**.govt.nz/system/files/.../**ethnicity**data**protocols**.pdf

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

1. Explain third bullet point of page 3 “excipient”.

Decision

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

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| **9** | **Ethics ref:** | **15/NTA/106** |
|  | Title: | JenaValve AS NZ Study |
|  | Principal Investigator: | Dr Mark Webster |
|  | Sponsor: | JVT Research and Development Corporation |
|  | Clock Start Date: | 30 July 2015 |

John Ormiston (co-investigator) 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) confirmed these valves have been in use for at least 10 years.
2. The Researcher(s) explained that transcatheter aortic valve implantation (TAVI) carries fewer risks than other treatments for high surgical risk patients. There are many benefits including lower death rates, less time in hospital and no need for full sedation as the procedure occurs under local anesthetic.
3. The Researcher(s) stated once the price of the study treatment drops it will be an accessible treatment.
4. This valve potentially fixes leaking of the heart.

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 how participants are recruited. Researcher(s) explained that there are meetings that involve a range of clinicians who discuss treatment options of their patients – for instance those who are high risk for surgery but suitable for the study. They will be approached and consented for the study or may refuse to participate. This will likely be at the time where clinicians would discuss what valve the patient will have. The Researcher(s) added that potential participants have time to talk to family but not their general practitioner. The potential participant usually has overnight to consider participation.
2. The Committee asked who would take them through consent process. The Researcher(s) stated their cardiologist.

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

1. The Committee noted withdrawal statement is not entirely true – once you have the valve you can’t remove it – please clarify for participants.
2. Page 2 – comparison between standard care –calling participants ‘high risk for surgery’ suggests that they should participate. Reword to ‘we only offer this to people who are high risk for surgery’ rather than suggesting that the alternative is a high-risk surgery, which could be coercive.
3. R.4.1.1 – incidental findings – put this information in the Participant Information Sheet
4. Describe TAVI systems – why it is different, better and why we want to study it.
5. Page 5 contains a list of TAVI specific risks and then it states that there are no additional risks. Please review.
6. Page 7 – The Committee notes that the study is not able to stop study for purely commercial interests.
7. ACC wording – use HDEC template for commercially sponsored trials compensation wording.

Decision

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

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| **10** | **Ethics ref:** | **15/NTA/107** |
|  | Title: | Improving diabetes outcomes for Māori in Whangaroa |
|  | Principal Investigator: | Dr Jennifer Reid |
|  | Sponsor: | University of Auckland |
|  | Clock Start Date: | 30 July 2015 |

Jennifer Reid (CI) and Aneka Anderson (Co-investigator) 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 Mr Kerry Hinii declared a potential conflict of interest (a study advisor is a DHB Board Committee member), and the Committee decided to have them stay in the room and participate in the meeting.

Summary of Study

1. The Committee thanked the researchers for their application. It was an interesting and important application.
2. The Committee commended the Participant Information Sheet.

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 the study focuses on poorly managed diabetes. Maori in this area have some of the worst outcomes in New Zealand.
2. The first stage is only about information gathering – primary and secondary data. From this information they plan to design an intervention to change the outcomes.
3. The Researcher(s) are looking at co-morbid depression. Anecdotally in this small areas all Maori diabetics have poorly managed glucose control, and most appear to have a clinical diagnosis of depression (as reported by the mobile nurse working with this group of patients).
4. The Researcher(s) explained that the second stage is to develop an intervention..
5. The Researcher(s) explained that she (CI) is funded for 3 years.
6. The Researcher(s) confirmed this application only concerned phase I of the project.
7. The Committee noted that providers and stakeholders were involved in the project. The Committee queried whether these people self selected to be involved? The Researcher(s) explained that there are not many providers available in this area. Those involved are from a range of areas including housing, rheumatic fever, ACC and primary care.
8. The Researcher(s) discussed the housing and economic context of the participant groups. The Researcher(s) want to look at how we can address how these issues impact management of diabetes.
9. The Researcher(s) noted that there is an advisory committee for the project.
10. The Committee queried how poverty and housing relates to the study question – on depression and diabetes. The Researcher(s) explained that they are interested in the links between diabetes and depression and poverty during childhood, impoverished fetal environments, high stress environments –all related to the social determinants of health. This geographical area is a microcosm of these features.
11. The Researcher(s) clarified they were not looking at a patient level (deficit model), but at a system level. Particularly how can they can change policy at a government level.
12. The Committee queried if data can be generalized to wider areas? The Researcher(s) explained it might be applicable to Maori – primarily rural – but not for wider population of New Zealand.
13. The Committee queried what management plan is in place for identifying suicidal ideation or severe depression (as a result of administering the interviews or questionnaires). The Researcher(s) explained that the results of these questionnaires aren’t diagnostic tools and couldn’t be shared with Whangaroa Health. The Researcher(s) have a group of advisors who will review the scores and will make an assessment. Someone from the study team will then contact the participant (who will have consented to this). If it was thought important to contact a doctor too the participant should consent to this prior to disclosure.
14. The Committee noted the high level of suicide in this population. The DHB could provide resources including the emergency response teams for assisting with risk management. Engagement with the local DHB as a stakehold was recommended and their inclusion in safety management planning.
15. The Committee queried whether it was possible for a person to refuse consent to having any depression risk notified to others – would this preclude them from participation? The Researcher(s) stated it did not preclude them.
16. The Researcher(s) clarified that identifying child abuse or clinical adverse findings will not be ignored and if a participant does not consent to acknowledging that these will be reported they should not participate.
17. The Committee queried whether there should be a Participant Information Sheet in Maori. The Researcher(s) explained that it was seriously considered, but very difficult. Past studies had very low requests for Maori language PIS. The Researcher(s) added that there are issues with functional language.
18. The Committee queried what Kaupapa Maori involved. The Researcher(s) explained that it was a Maori research methodology that involved Maori worldviews and methods.
19. The Researcher(s) explained that these methodologies were used in the consultation process, which involves relationship building over time.
20. The Committee queried how stigma would be managed? The Researcher(s) explained that the community requested that the research occurs – they know they have diabetes and want help. The Researcher(s) explained that Kaupapa Maori methodologies reject deficit blaming – it removes blame from the community and resituates it higher up, such as the health system.
21. Please store health information generated from the study for 10 years.
22. Please address researcher safety – how you will ensure researchers are safe. The Researcher(s) noted this is outlined in the memorandum of understanding. Please note this in the HDEC documents.
23. The Committee noted any identification of illegal activity is vague – be specific about what would be reportable / notifiable and what was going to be kept confidential under usual limits of confidentiality processes (eg disclosure of drug taking would be considered confidential to the research and not be disclosed).
24. The Researchers were invited to consider the potential implications of sharing of patient level information with Housing NZ or other stakeholders as currently outlined in the PIS. There could be unintended consequences of this action.
25. The Researchers are also invited to consider the potential disclosure of sensitive information in interviews in the presence of potentially wider whanau. This may or may not be problematic.

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

1. Please add some information on rights in the Participant Information Sheet such as right to withdraw or right to stop interviews at any time.
2. Number pages and add version number
3. Add information about potential identifiably due to small sample size.

Decision

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

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| **11** | **Ethics ref:** | **15/NTA/108** |
|  | Title: | JenaValve AR NZ Study |
|  | Principal Investigator: | Dr Mark Webster |
|  | Sponsor: | JVT Research and Development Corporation |
|  | Clock Start Date: | 30 July 2015 |

John Ormiston (co-investigator) 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) confirmed these valves have been in use for at least 10 years.
2. The Researcher(s) explained that transcatheter aortic valve implantation (TAVI) carries fewer risks than other treatments for high surgical risk patients. There are many benefits including lower death rates, less time in hospital and no need for full sedation as the procedure occurs under local anesthetic.
3. The Researcher(s) stated once the price of the study treatment drops it will be an accessible treatment.
4. This valve potentially fixes leaking of the heart.

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 how participants are recruited. Researcher(s) explained that there are meetings that involve a range of clinicians who discuss treatment options of their patients – for instance those who are high risk for surgery but suitable for the study. They will be approached and consented for the study or may refuse to participate. This will likely be at the time where clinicians would discuss what valve the patient will have. The Researcher(s) added that potential participants have time to talk to family but not their general practitioner. The potential participant usually has overnight to consider participation.
2. The Committee asked who would take them through consent process. The Researcher(s) stated their cardiologist.

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

1. The Committee noted withdrawal statement is not entirely true – once you have the valve you can’t remove it – please clarify for participants.
2. Page 2 – comparison between standard care –calling participants ‘high risk for surgery’ suggests that they should participate. Reword to ‘we only offer this to people who are high risk for surgery’ rather than suggesting that the alternative is a high-risk surgery, which could be coercive.
3. R.4.1.1 – incidental findings – put this information in the Participant Information Sheet
4. Describe TAVI systems – why it is different, better and why we want to study it.
5. Page 5 – TAVI specific risks. Then it states that there are no additional risks. Review for contradiction.
6. Page 7 – The Committee notes that the study is not able to stop study for purely commercial interests.
7. ACC wording – use HDEC template for commercially sponsored trials compensation wording.

Decision

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

## General business

1. The Committee noted the content of the “noting section” of the agenda.
2. The Secretariat gave the HDEC an update on training and on-going plans.
3. The Chair reminded the Committee of the date and time of its next scheduled meeting, namely:

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

The following members tendered apologies for this meeting.

* Dr Brian Fergus
* Ms Susan Buckland

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 5.45pm