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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 21 August 2018 |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

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| **Time** | **Item of business** |
| 1:00pm | Welcome |
|  | Confirmation of minutes of meeting of 19 June 2018 |
| 1:30pm | New applications (see over for details) |
|  | I 18/NTA/119  ii 18/NTA/132  iii 18/NTA/123  iv 18/NTA/125  v 18/NTA/126  vi 18/NTA/129  vii 18/NTA/136  viii 18/NTA/130  ix 18/NTA/121  x.17/NTA/12 |
| 5:00pm | General business:   * Noting section of agenda |
| 5:30pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Brian Fergus | Lay (consumer/community perspectives) | 11/11/2015 | 11/11/2018 | Present |
| Dr Karen Bartholomew | Non-lay (intervention studies) | 13/05/2016 | 13/05/2019 | Present |
| Dr Christine Crooks | Non-lay (intervention studies) | 11/11/2015 | 11/11/2018 | Apologies |
| Dr Kate Parker | Non-lay (observational studies) | 11/11/2015 | 11/11/2018 | Present |
| Dr Catherine Jackson | Non-lay (health/disability service provision) | 11/11/2016 | 11/11/2019 | Present |
| Ms Toni Millar | Lay (consumer/community perspectives) | 11/11/2016 | 11/11/2019 | Present |
| Ms Rochelle Style | Lay (ethical/moral reasoning) | 14/06/2017 | 14/06/2020 | Presemt |

## Welcome

The Chair opened the meeting at 1:07pmand welcomed Committee members, noting that apologies had been received from Christine Crook.

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 21 July 2018 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **18/NTA/119** |
|  | Title: | HEAD Study |
|  | Principal Investigator: | Dr Sinan Kamona |
|  | Sponsor: |  |
|  | Clock Start Date:: | 09 August 2018 |

Dr Sinan Kamona 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 aims to provide a wider inter-regional and international perspective on the epidemiology of non-trauma related headache and its patterns of investigation, treatment and outcome.

Summary of ethical issues (resolved)

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

1. The Researcher stated that they would follow 100 patients presenting to Emergency Department (ED) with headaches to see what their outcome is, what investigation and management is being done and, what the diagnostic outcome is.
2. The Committee were concerned that no consent to take part is being sought from participants so questioned why this study is not being done as a retrospective audit.

The Researcher(s) explained that they want to identify participants prospectively as they feel they would more likely correctly identify participants and if necessary they would do some retrospective data completion. They felt that with retrospective audit the chance of missing participant’s increases. The Researcher hopes (though not guaranteed) to introduce the SNOWMED presentation complaints list to their electronic system which would potentially make the identification of participants more robust although with this they would want prospective identification of data.

1. The Committee queried what would define a hospitalisation event and the period that follow up would be carried out to.

The Researcher clarified that re-presentation within 72hrs would be considered as another hospitalisation event. They felt that it would be sufficient to only follow participants to discharge and get a discharge diagnosis.

1. The Committee queried if the study would be able to get the data it needs at discharge.

The Researcher stated that it should. Within one to two days from discharge the notes are scanned and the research team are able to finalise data retrospectively from clinical notes.

1. The Committee wanted to know if this study is run as a retrospective audit, the number of participants that would be missed.

The Researcher explained that it is an electronic problem for them as their current practice does not have standardised coding for presentation, it is all free text. They would have to create an algorithm to pick participants versus what they would hope to do that is, have research nurses in the department 12 hours/day to prospectively identify participants. It would be hard to know for certain what percent of participants would be missed.

1. The Committee felt that if the study was being done prospectively with research nurses, 12 hours of the day would still be missed so potentially less participants would be missed by conducting a retrospective study.

The Researcher could not confidently commit to a figure as the research team has not done a prospective analysis for headaches. The Researcher could however provide an estimate based on a prospective analysis they had done for chest pains. For this, missed participants had a variance of around 5-10%. The Researcher proposed that headaches may have a similar variance.

1. The Committee stated that for it to approve a prospective study without consent, would require the researchers to prove that their study would be in the best interests of participants (*Code of Health and Disability Services Consumers’Rights, Right 7(4)*). However, this is only so for intervention studies.
2. The Committee emphasised that in New Zealand it is difficult to receive approval from HDEC for opt-out studies.
3. The Researcher explained that they want to include all participants that present with non-traumatic headache which would include those with potentially lower Glasgow Coma Scale (GCS) who are not able to consent and may be in significant pain so it may be difficult for them to understand, at the time. The Researcher was concerned that they may also miss out on participants who are unable to provide consent due the severity of their illness/pain and this is a group they want to include.
4. The Committee questioned the type of information being collected that is, how long are participants followed up, what information needs to be collected and whether its collection ceases at discharge or carries on afterwards.
5. The Researcher advised that they would only follow participants until a discharge diagnosis is achieved or death. They would look at past medical history, current presentation, demographics, medications, clinical history of present illness, examinations, investigations and, final diagnosis and treatment in the ED. There are some descriptive studies from Australia and United Kingdom but none in New Zealand. This data collection will allow the researchers to have their own data, collate and look at it and, compare it to pooled data from the study group. This would help to describe their own practice within their department and potentially across New Zealand based on the interest of other EDs to join the data collection. They plan to also make data comparisons with Australia and other sites around the world.

The researchers will look at the Ottawa Subarachnoid Haemorrhage Rule and apply it to their own group of participants to see if it safe.

1. The Committee questioned where data would be kept and whether it would be kept in an identifiable form.

The Researcher explained that data would be kept at the hospital and only clinicians and the audit group will have access. Data would be de-identified before it is shared with other sites. To protect identity, all participants will be assigned a number which is matched to a secure password. NHIs will be matched to these passwords. Data will be kept for 7 years and securely stored either electronically or in a locked cupboard.

The Committee reminded the researcher that data should be kept for a minimum of 10 years *(Health (Retention of Health Information) Regulation 1996)*

1. The Committee queried if data would be sent away to Australia.

The Researcher stated that only de-identified data would be sent away to the coordinating centre in Australia. Each site analyses their own data and would have no access to each other’s.

The Researcher clarified that the only information collected on participants would be their ethnicity, age and gender. No date of births or NHIs are collected.

1. The Committee did not receive the full section on data definitions in appendix one and requested the Researcher email this through to [hdecs@moh.govt.nz](mailto:hdecs@moh.govt.nz). HDEC’s administration team will manually add this document to the submission.
2. The Researcher stated they would spend one month on prospectively identifying participants and two weeks to finalise data.

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 ensure all stored health information is kept for a minimum of 10 years.
2. The Committee stated that the study should be conducted in two separate parts;
3. prospectively identify patients for a screening log
4. then complete the data collection retrospectively
5. Please provide justification for not seeking consent for the access of retrospective data

Decision

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

* Please ensure all stored health information is kept for a minimum of 10 years (*Health (Retention of Health Information) Regulation,1996*).
* The Committee stated that the study should be conducted in two separate parts,

1. prospectively identify patients for a screening log
2. then complete the data collection retrospectively

* Justification is required for not seeking consent for the access of retrospective data (Ethical Guidelines Observational Studies, paragraph *6.43*)

This following information will be reviewed, and a final decision made on the application, by Dr Kate Parker & Ms Toni Millar.

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| **2** | **Ethics ref:** | **18/NTA/132** |
|  | Title: | The DynamX Sirolimus Study |
|  | Principal Investigator: | Dr Mark Webster |
|  | Sponsor: | Elixir Medical Corporation |
|  | Clock Start Date: | 09 August 2018 |

Mrs Jan Burd and Ms Mandy Fish were present in person for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. Traditional metal stents rigidly splint the vessel wall preventing normal vessel motion (expansion and contraction). This can cause abnormal haemodynamics and wall shear stress. One solution for this was the introduction of fully bioresorbable stents, which dissolve completely over time, allowing a return to normal vessel motion. However these stents do have some limitations.
2. The study sponsor has designed a new generation of stent called the DynamX stent. This stent has expansion segments in the stent pattern. The expansion segments are designed to disengage approximately six months after the stent is implanted allowing the stent to expand and contract with the movement of the artery. The stent is therefore expected to perform like a metallic stent for vessel support, with the benefit of performing like the bioresorbable stent for vessel motion.
3. The purpose of this research study is to confirm the safety and performance of the DynamX Sirolimus Eluting Coronary Bioadaptor System (SECBS).
4. The stent trial is technically a first in human. Up to 30 participants will be involved in the study at up to 10 clinical sites in New Zealand. All participants enrolled in the study will be undergoing coronary artery stenting as part of standard clinical care. Participants enrolled in the study will be followed up 1, 6 and 12 months after the stent implant procedure. The 6 month follow up visit will include an angiogram to assess the study stent.
5. Within the study an IVUS (intravascular ultrasound) Sub-Study involving 15 participants will be conducted. Participants in this sub-study will have IVUS imaging of the stent at the baseline and 6 month follow up angiograms.

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) stated that Dr Mark Webster (CI) is not part of the development of the product and is part of the steering committee.
2. The Committee queried if any adverse events have occurred in the European trial.

The Researcher(s) advised there are approximately 45 enrolled in Europe, the stent is performing as expected and there have been no device related adverse events. It is still early days though.

1. The Committee questioned if training would be set up for the use of the device.

The Researcher(s) responded that it hasn’t yet but it will.

1. The Researcher(s) stated that essentially the study is a safety and performance one with a view to extend it to a later phase study.
2. The Committee queried if the New Zealand sites would be involved in the IVUS.

The Researcher (s) informed that IVUS will be available to all sites but only the first 15 participants enrolled will be part of it. It will be determined by which sites are up and running first.

1. The Committee asked if the IVUS would take much longer than the main study and what risks are associated with it.

The Researcher(s) responded that the risks are noted on page 4 but its main side effect is when the fibre optic wire goes up through the vessel it can sometimes create a bit of a spasm.

The Researcher(s) clarified that IVUS is a standard imaging modality and not an investigational product.

1. The Committee questioned if the application of the stent would take longer than the commercially available stent.

The Researcher(s) stated that the IVUS will take 5-10minutes and the stent deployment and delivery system is similar to the commercially available stent it is based on.

1. The Committee asked for clarification on what is follow up standard of care and what is not.

The Researcher(s) advised that standard of care follow up is 4-6weeks, the angioraphic follow up is study specific and is always symptom driven. The 6 & 12 months follow ups are additional to standard of care. They will try to have the 30 day follow up within the standard follow up period.

1. The Committee questioned if the scans will be in a de-identifiable form when sent to the sponsor

The Researcher(s) confirmed that they would be and only identifiable by study number.

1. The Researcher(s) stated that images will be sent to a core lab in Brazil where baseline image will be compared to the 6 month image. This is to gain an idea of how the stent is performing. The images will not be used for machine learning and is purely for end point analysis.
2. The Committee questioned the extra blood samples taken.

The Researcher(s) advised that this was only for participants that did not have their blood drawn during standard of care. This blood sample will be used to look at renal function which is standard for angiographs and will not be kept for any other reasons.

1. The Committee questioned if there would be incidental findings.

The Researcher(s) felt that potentially there could be as participants would have ionised radiation and ECGs. Should they occur, the 6 month follow up renal check could be the time they appear.

1. The Committee questioned if individual results would be available to participants.

The Researcher(s) confirmed that they would.

1. The Committee noted that the latest HDEC advised ACC wording is only being partially used in the study’s Participant Information Sheet (PIS). The Committee advised that this would be acceptable for this study but for other studies to come, the full version of the update is to be applied.
2. The Committee questioned the absence of stent risks in the PIS.

The Researcher(s) explained that stent risks would be consented separately under the stent procedure so participants are aware of risks before they are screened for the study.

1. The Committee appreciated the face to face discussion on the experimental stent but found its explanation in the PIS to be complicated. The Committee suggested the use of a diagram to simplify things.

The Researcher(s) explained that the diagrams they have are more complex than simple so felt it was better not to include them. The research team finds the best way to simplify things for participants is to talk through the PIS with them and have a dummy stent on hand.

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 advised that it needs to be made clear to sponsors that a study cannot be terminated for commercial reasons

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

1. Add a section to PIS on the process of receiving study information.
2. Participants should be informed of their right to access and correct their data.
3. Point 15 (above) needs to be clearly explained in lay language.
4. The Consent form is reviewed for truly optional statements as only those should have yes/no tick boxes next to them (ie, if a participant selects ‘no’ they can still take part in the study).
5. Information about scans/images being sent overseas is only mentioned in the Consent form. It should be detailed in the PIS too. Please correct this and advise participants of the measures that will be taken to protect their privacy.
6. The benefits section, page 4 needs to include a line to say that the stent may potentially have no benefit and that once it is put in, it cannot be taken out. The stent not being able to be removed once in, should also be added to the withdrawal section.
7. Be clear about the difference in standard of care follow up and study specific follow up. A table could be used to clarify this
8. The Committee noted that it is not clear up front that this study is a first in human trial. This should be made clearer earlier in the document.
9. Please include a brief statement in the PIS about the return of individual results and include an option in the consent form.
10. Please include a brief explanation in the PIS about incidental findings.
11. Please upload a consent form for the sub-study.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the committee *(Ethical Guidelines for Intervention Studies para 5.4,page11)*
* A study cannot be stopped simply for commercial reasons or public relations (*Ethical Guidelines for Intervention Studies, para 6.65*)

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

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| **3** | **Ethics ref:** | **18/NTA/123** |
|  | Title: | A study looking at the effects of the trial drug Selonsertib on kidney function, in adults with chronic kidney disease. |
|  | Principal Investigator: | Dr. Richard Robson |
|  | Sponsor: | Gilead Sciences Pty Ltd |
|  | Clock Start Date: | 09 August 2018 |

Dr Richard Robson 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. Selosertib (SEL) is being developed for the treatment of diabetic kidney disease.
2. The study aims to assess kidney function before, during and after SEL.

Summary of ethical issues (resolved)

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

1. The Committee questioned if the study is a Phase 1 trial.

The Researcher stated that it is not really as it has been used in a number of clinical trials involving both patients and volunteers.

1. The Committee questioned how recruiting would be done.

The Researcher explained that there are 10 sites around the world and 2 in New Zealand. One site in Auckland and the other in Christchurch. Both sites will be using the nephrology contacts to recruit for the study– ie, patients known to Dr Robson in Christchurch or Dr Collins in Auckland.

Drs Robson and Collin will give patients a brief outline of what is involved and the research nurses then follow up to see if there is interest or not.

1. The Committee queried why tissue was being collected for Future Unspecified Research (FUR)

The Researcher responded that they wished to see if there are any genetic markers that affect drug response. The Researcher confirmed that it is mandatory to give tissue for the main study but optional for FUR. The study will have separate consents for the two. If participants consent for the main study then tissue will be taken and used to measure both new medicine and Iohexol.

1. The Committee queried if participants will be videoed during the study.

The Researcher replied that video cameras are in the patient/volunteer lounge but they would not be used as part of the study.

1. The Researcher confirmed that medical records will not be looked at.
2. The Committee asked for reassurance that there are no other Serious Adverse Events (SAEs).

The Researcher confirmed that the study is free from significant SAEs. The SAEs that were experienced, were in equal amounts in both the placebo and the active.

1. The Committee asked what adverse events are associated with Iohexol and to what likely frequency.

The Researcher stated that if any, at very low frequency as it is used as a contrast agent by radiologists every day. The only risk is if you have an allergic reaction which tends to be uncommon but can happen.

1. The Researcher confirmed the types of diseases this drug can be applied to that is, diabetes and possibly transplant medicine. Diabetic kidney disease is a subset of chronic renal disease. Diabetic patients will not be excluded from the trial. It is likely that 20-30% of participants will be diabetic. They will have to meet the inclusion/exclusion criteria.

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 check and confirm with your sponsor that there is a mechanism in place for Consent for Future Unspecified Research, in other words, that data management and governance allow a participant’s choices regarding the parameters of the FUR to be complied with and respected.

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

Main PIS/CF

1. Please state early on why participants are chosen, what the study is about and that there will be no potential benefit in the study. The reference to Iohexol in the second paragraph on page 1 of the PIS is confusing. The purpose section of the PIS needs to be improved to provide a clearer explanation of the research.
2. The Committee noted on page 2 of the Participant Information Sheet the statement, “study will help to show that the drug doesn’t injure the kidney”; this seems to pre-suppose the outcome of study. It would be more appropriate to state, “study will help to show whether or not the drug injures the kidney”.
3. Please state where participants will stay overnight.
4. The Committee requested that the PIS state that participants are required to fill in a food diary to record what they ate for breakfast, lunch and dinner over the 9 days of the study.
5. Please change the line, “Samples will be collected to see how much virus is in the blood” to “Samples will be collected to see if virus is in the blood”.
6. Participants should be aware that testing for viral infection of Hepatitis B, C and HIV are notifiable so if they test positive their results will be shared with the public health authorities.
7. Be clear about where samples will be stored overseas (page 8) – currently, the PIS only states where the samples will be analysed.
8. State what tests will be part of the routine health test so participants are re-assured of what is being looked at (eg, renal and liver function test).
9. State that some safety blood tests will be done in New Zealand and that samples will destroyed and not stored.
10. Statements about side effects should include frequency of occurrence, eg, Common, 10% and severity
11. The Committee noted that a side effect of Iohexol is death. However, this is extremely rare so please include a statement to that effect and also state that Iohexol is commonly used as medicine in radiology
12. State that both study sites are equipped to deal with allergic reaction if it happens.
13. Please apply the following HDEC’s Commercial sponsor compensation statement (as found in the HDEC PIS/CF template):

*As this research study is for the principal benefit of its commercial sponsor [insert name], if you are injured as a result of taking part in this study you* ***won’t*** *be eligible for compensation from ACC.*

*However, [insert name] has satisfied the [ insert name] Health and Disability Ethics Committee that approved this study that it has up-to-date insurance for providing participants with compensation if they are injured as a result of taking part in this study.*

*New Zealand ethical guidelines for intervention studies require compensation for injury to be at least ACC equivalent. Compensation should be appropriate to the nature, severity and persistence of your injury and should be no less than would be awarded for similar injuries by New Zealand’s ACC scheme.*

*Some sponsors voluntarily commit to providing compensation in accordance with guidelines that they have agreed between themselves, called the Medicines New Zealand Guidelines (Industry Guidelines).These are often referred to for information on compensation for commercial clinical trials. There are some important points to know about the Industry Guidelines:*

* *On their own they are not legally enforceable, and may not provide ACC equivalent compensation.*
* *There are limitations on when compensation is available, for example compensation may be available for more serious, enduring injuries, and not for temporary pain or discomfort or less serious or curable complaints.*
* *Unlike ACC, the guidelines do not provide compensation on a no-fault basis:*
* *The Sponsor may not accept the compensation claim if:*
* *Your injury was caused by the investigators, or;*
* *There was a deviation from the proposed research plan, or;*
* *Your injury was caused solely by you.*
* *The injury was caused by <<NAME OF COMPARATOR DRUG>> (include only if holds true for specific study)*

*An initial decision whether to compensate you would be made the by the sponsor and/or its insurers.*

*If they decide not to compensate you, you may be able to take action through the Courts for compensation, but it could be expensive and lengthy, and you might require legal representation. You would need to be able to show that your injury was caused by participation in the trial.*

*You are strongly advised to read the Industry Guidelines and ask questions if you are unsure about what they mean for you.*

*If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.*

1. Please amend the wording on page 16 to refer to New Zealand rather than “your country’. The PIS should reflect the fact that the participants reading the PIS are located in NZ.
2. Use the HDECs consent form template as the current CF has some statements missing (eg, samples will sent overseas and stored for 15 years, will participants get individual results back? If so, this also needs to be mentioned in the PIS, similarly with any expected abnormal/incidental findings and how these will be dealt with) PIS/CF template can be accessed at <https://ethics.health.govt.nz/> under the Quick Links section.
3. The PIS sets out (on page 16) a number of purposes for which participants’ data will be used for the purposes of the study. The PIS also states (on page 17) that participants’ data will be used for ‘additional unanticipated medical and/or scientific research projects in the future relating to your disease or similar diseases and/or development of the study drug …”(page 17). This is broad unspecified research. The consent form must include, in a separate section, a statement to ensure that participants are aware that their data may be used for purposes outside the research and that they consent to it.
4. Please make sure risks and benefits, privacy and confidentiality are included too (see HDECs PIS/CF template). For example, the PIS should also include a statement to the effect that *There is a very small risk that the üse of your de-identified data might allow you to  be re-identified, even if they don’t include your name.  We have  taken steps to guard against that happening by using a unique code to protect your confidentiality.  However, people may come up with new ways of tracing information in the future.*
5. Add the following Maori tissue statement:

*You may hold beliefs about a sacred and shared value of all or any tissue samples removed. The cultural issues associated with sending your samples overseas and/or storing your tissue should be discussed with your family/whanau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult prior to participation in research where this occurs. However, it is acknowledged that individuals have the right to choose.”*

1. .The application (para r.3.7)) states that results will be data based and linked to participant information This needs to be explained in the PIS if it relates to linking with a database other than the study database including an explanation of what any linking will be used for and how it will be done. Risks involved with linking data should also be explained to participants if external databases are proposed to be used and a separate section should be included in the consent form whereby participants expressly consent to such linking
2. The application (para r.3.11) states that tissue will be transferred to another tissue bank. An explanation of these matters must be included in the PIS, including the location of the tissue bank and what purposes the tissue might be used for – eg, future unspecified research? A section relating to this matter must also be included in the consent form.
3. It should be mentioned early in the PIS that the study is sponsor-led by Gilead.

Future Unspecified Research PIS/CF:

1. State where other samples be stored and if they will be de-identified. Will they be stored with other health information about participants (eg, diagnosis).
2. Please include as part of the genomic testing, the risk of potential re-identification.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the committee *(Ethical Guidelines for Observational Studies para 6.10)*
* Please refer to Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes to ensure you comply with requirements (<https://www.health.govt.nz/publication/guidelines-use-human-tissue-future-unspecified-research-purposes-0> )

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This following information will be reviewed, and a final decision made on the application, by Dr Catherine Jackson & Dr Brian Fergus

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| **4** | **Ethics ref:** | **18/NTA/125** |
|  | Title: | OAKS |
|  | Principal Investigator: | Dr James Borthwick |
|  | Sponsor: | Apellis Pharmaceuticals Pty Ltd |
|  | Clock start Date | 09 August 2018 |

Dr James Borthwiks 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. Participants will receive the investigational product, APL2 15mg/0.1mL, via intravitreal injection (injection into the eye), or they will receive a sham injection.
2. Participants are injected either monthly or every other month for 24 months, followed by a 6 month follow up period.
3. The primary objective of the trial is to evaluate the change from Baseline

to Month 12 in total area of GA Lesions as Measured by Fundus Autofluorescence(FAF)

1. The secondary objective is to determine the incidence and severity of ocular and systemic treatment emergent adverse events. [Time Frame: 24 months].

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 would like clarification of groups in the study and the randomisation process. In particular, please explain whether the sham procedure involves an injection into the eye – there is confusion in the PIS (eg, pages 3 and 12) and the application (eg, para r.1.1)
2. The Questionnaire document refers to mental health. Please explain the safety process in place should a participant identify a mental health history.
3. How is ethnicity going to be collected?
4. What is the termination process if a participant gets worse? Will they come off the study or if on placebo, be transferred to the active drug?
5. The Committee noted the reference to additional study material (page 8 of PIS). Please explain what this is.
6. Please explain to the Committee what the following statement means; “your specimen analysis will not be provided to you or study staff unless required by law”. (page 5 of PIS).

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

1. Take term “race” out on pages 5 and 10.
2. Explain visual acuity in lay terms. The words sharpness/clarity could be used.
3. For the Labs, what are the bloods and urine for? (page 5, PIS) Please explain PK and compliment.
4. Selected sites and e-diary are mentioned. Please explain what is actually being done and what the e-diary is for.
5. Please review all acronyms and ensure they are explained.
6. Section 10, page 15 talks about samples. Where are they going? Only Singapore is mentioned. Participants are entitled to know where their samples are being sent. The Committee do not approve the selling of samples.
7. Additional consent is mentioned on page 16. Is this for the Genetic PIS? Please include the word optional to the title of this additional consent.
8. Take everything out about sub-study and state that there will be an optional sub-study.
9. What images are being taken? The PIS refers only briefly to the taking of images (page 16) – further explanation is required – for example, Is it on the procedures and will it identify participants? Will the images be sent overseas? If so, where? The potential risks of re-identification should be included in the PIS depending upon the identifiability of the images and what steps will be taken to protect the privacy of participants (eg, de-identification). The PIS states that the images may be used for future research. What kind of research? A separate section relating to the images should be included in the consent form so participants expressly consent to their use.
10. Withdrawal can be made verbally. Written withdrawal is not required.
11. Recruitment is not explained properly.
12. Please include the following Maori tissue statement;

*You may hold beliefs about a sacred and shared value of all or any tissue samples removed. The cultural issues associated with sending your samples overseas and/or storing your tissue should be discussed with your family/whanau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult prior to participation in research where this occurs. However, it is acknowledged that individuals have the right to choose.”*

1. Please state if samples can be removed and destroyed if participants request so.
2. Death is mentioned as an allergic reaction. Please correct this and, if death is a risk

then this should be stated.

1. Tabulate the days of study to make it easier to follow. Can participants drive home afterwards?
2. Please include HDEC’s updated Commercially sponsored compensation statement (as noted in the HDEC PIS/CF template);

“As this research study is for the principal benefit of its commercial sponsor [insert name], if you are injured as a result of taking part in this study you **won’t** be eligible for compensation from ACC.

However, [insert name] has satisfied the [ insert name] Health and Disability Ethics Committee that approved this study that it has up-to-date insurance for providing participants with compensation if they are injured as a result of taking part in this study.

New Zealand ethical guidelines for intervention studies require compensation for injury to be at least ACC equivalent. Compensation should be appropriate to the nature, severity and persistence of your injury and should be no less than would be awarded for similar injuries by New Zealand’s ACC scheme.

Some sponsors voluntarily commit to providing compensation in accordance with guidelines that they have agreed between themselves, called the Medicines New Zealand Guidelines (Industry Guidelines).These are often referred to for information on compensation for commercial clinical trials. There are some important points to know about the Industry Guidelines:

* On their own they are not legally enforceable, and may not provide ACC equivalent compensation.
* There are limitations on when compensation is available, for example compensation may be available for more serious, enduring injuries, and not for temporary pain or discomfort or less serious or curable complaints.
* Unlike ACC, the guidelines do not provide compensation on a no-fault basis:
* The Sponsor may not accept the compensation claim if:
* Your injury was caused by the investigators, or;
* There was a deviation from the proposed research plan, or;
* Your injury was caused solely by you.
* The injury was caused by <<NAME OF COMPARATOR DRUG>> (include only if holds true for specific study)

An initial decision whether to compensate you would be made the by the sponsor and/or its insurers.

If they decide not to compensate you, you may be able to take action through the Courts for compensation, but it could be expensive and lengthy, and you might require legal representation. You would need to be able to show that your injury was caused by participation in the trial.

You are strongly advised to read the Industry Guidelines and ask questions if you are unsure about what they mean for you.

If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.

1. The consent forms need to be amended to use NZ terminology – “Protected Health Information” is not such a term and it also has not been defined in the PIS.
2. In the section which explains what will happen to participants’ information, please explain that data protection in other countries may be different to and offer less protection to participants than in NZ
3. Please change your statement‘ your identity will never be revealed” (page 19) to ”your identity will not be published in a form that could reasonably be expected to identify you “
4. Please include a statement in the PIS about return of individual results and include a section in the consent form. Please also include a section which provides participants with the option to receive results of the study if they wish

Genetic study and Clinical Repository sub-study PIS

1. Please clarify whether there is a difference between the proposed banking of samples (section 12, page 5) and the clinical biorepository (page 3). Where are the banks/repositories located? If it is the same put it in one section and be clear that it is broad consent (ie, consent to stored tissue for this and any other research)
2. Please include an explanation in the PIS about the possible risks of re-identification
3. Please state what other countries the samples will be sent to (page 5).
4. The consent form refers to three different types of consent for use of the genetic samples. These must be set out and clearly explained in the PIS.

Currently, the PIS says information will only be used for this research project (page 7) but the consent form refers to future unspecified research. On the other hand the clinical repository section says that samples can be used for any future research (page 5).

1. Please also confirm to the committee that the data management and governance of the biorepositories/banks are robust so as to ensure that participants choices are complied with and respected.
2. The consent form asks participants to consent to his or her doctors/health professionals releasing information to a currently unnamed institution concerning his or her condition. The institution must be named. Furthermore, an explanation about release of confidential health information should be included in the PIS. It should not appear for the first time in the consent form.
3. Please include the Maori tissue statement in the PIS
4. Please use HDECs Consent form template (<https://ethics.health.govt.nz/home> under the Quick Links section)
5. Please state that samples will be going overseas in the Consent Form.
6. Remove the last statement at the top of page 2 of the Consent form, “I understand if I decide to discontinue the study treatment, I may be asked to attend follow-up visits to allow collection of information regarding my health status……” This does not belong in this PIS.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the committee *(Ethical Guidelines for Observational Studies para 6.10)*
* Please ensure contingencies are in place should participants identify a mental health history (*Ethical Guidelines for Intervention Studies, paragraphs 5.37 & 5.38*)
* It is important that participants have an adequate understanding of information so they can make informed decisions. Participants should be protected from coercion, manipulation and other undue influence (*Ethical Guidelines for Intervention Studies, paragraphs 6.6-6.8*)

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

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| **5** | Ethics ref: | 18/NTA/126 |
|  | Title: | (duplicate) Teledermatology for scabies |
|  | Principal Investigator: | Dr Simon Thornley |
|  | Sponsor: | University of Auckland |
|  | Clock Start Date: | 09 August 2018 |

Dr Simon Thornley (CI) 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.

Catherine Jackson declared a potential conflict of interest, and the Committee decided that she could leave the room and not take part in the discussion or decision making for this application.

Summary of Study

1. In order to determine the burden of scabies in Auckland, an efficient method of making diagnosis is needed. Scabies is a difficult disease to diagnose accurately and misdiagnoses commonly occur.
2. Microscopy is required to identify key features of scabies; however, it is often not used by non-specialists. The infrastructure exists for teledermoscopy (taking pictures with a smartphone) to assist the diagnosis of scabies. Cheap cellphone lens attachments can be used to take a series of photos of lesions for review.
3. The study will assess the level of agreement between the gold-standard of identifying scabies and impetigo, dermatological assessment, and that of trained primary care practitioners, with or without supplemental teledermatology and specialist review of images and clinical information.
4. The findings of this study will then guide a designed survey of scabies prevalence in Auckland schools. If impetigo and scabies are found to be closely linked, this would have immediate clinical implications for the primary care treatment of scabies.
5. The information found should help define sociodemographic and geographic populations where treatment could be focused.

Summary of ethical issues (resolved)

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

1. The Researcher confirmed that demographics collected would be age, ethnicity and gender. Ethnicity categories will be based on the census question.
2. The Committee questioned if feedback has been received from Maori and Pasifika consultations.

The Researcher advised that no feedback has been received yet.

1. The Committee questioned if consultation had been undertaken with childcare centres in terms of input and how the trial might be effectively run.

The Researcher advised that one centre is very keen to have them. A good number of their children have a scabies issue and they would appreciate having a dermatologist on hand.

1. The Committee asked if the questionnaires would be administered by the childcare centre staff. The Researcher confirmed they would.
2. The Committee were concerned as childcare staff are not trained in administering questionnaires. Questions and answers made are detailed and there are privacy issues around these.
3. The Committee questioned the procedures in place to manage stigma in the day care environment.

The Researcher stated they would emphasise that scabies is treatable and is of a reversible nature. Once treated there will be no reason to continue to have scabies.

1. The Researcher confirmed that the sample number is limited by the size of the centre

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 use staff trained in administering questionnaires for the study, for example, the nurse, GP or dermatologist
2. The Committee requested that the HDEC peer review template be completed. The current copy uploaded has no comments in its body.
3. The Committee felt it is not appropriate for photographs to be used for machine learning during the pilot study and if the researchers wish to pursue this aspect of the research, much greater detail will need to be provided to the Committee.
4. The Poster just states free check-up but it must expressly refer to the study and that it is research. An amended poster must be uploaded for the committee’s review.
5. The letter for parents whose child is diagnosed with scabies should be reviewed by the Committee.
6. The Committee expressed concern about children undressing in front of a centre’s staff member in terms of privacy, especially if a child’s parent or care-giver is present when there is no need for the centre’s staff to be present. The researchers should consider how to manage the privacy aspects of the examination to minimise the number of people present and to maximise a child’s privacy. More information is also required in the PIS about the extent to which a child will need to be undressed and the measures that will be taken to protect a child’s privacy.
7. The Committee noted the inclusion of Impetigo in the Protocol title. Impetigo and Scabies are not similar conditions and this should be made clear. Please clarify if Impetigo will be treated as well.
8. The Committee questioned the $10 contribution and if it would be sufficient to treat a large family.
9. The Committee questioned what pictures would be taken and if they had the potential to identify the child.

The Researcher stated they would take regional pictures of the area and that they may potentially include the child’s face but very unlikely. The Researcher advised that the photos will be uploaded and kept on web portal provided by a teledermatology provider called First Check.

The Committee requested more information about First Check and, generally, what measures will be taken to ensure the security of the images particularly in relation to privacy protection. This detail should also be noted in the Participant Information Sheet (PIS).

1. Please provide a very simple information sheet and assent form for young children that should very simply explain their participation in the study. Guidance on assent can be found at <http://ethics.health.govt.nz/guidance-materials/assent-guidance>.
2. Please include an image of the microscope at the end of the phone in the Assent forms. Please ensure the image is at a level that the targeted age will relate to/understand.
3. Please ensure each child’s data/information is allocated a unique study number for confidentiality and ensure that this number is used on all study data and images rather than a child’s name or initials.
4. The Committee questioned how recruitment will be conducted.

The Researcher advised that parents would have to consent first before children can be involved.

Information Sheets would be provided either in a paper or digital form (via a website).

The Committee requested more information on the website and recommended that the research team be available to assist and talk the parents/children through the information sheets.

1. The Committee advised that if you want to test as part of the feasibility question, if people will take part in study, then more health literacy is required (eg,cohort, population, appearance)

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

1. The phrase “burden of scabies” should be avoided, as requested by the Southern HDEC when it reviewed this study.
2. Please make it clear that the examination will be made by 3 people and photos will be taken and reviewed by a fourth person (Dermatologist). Encourage parents/caregivers to be there for support.
3. There seems to be a mix up between “your” and “your child”. Please check this for accuracy.
4. The PIS currently mentions that a child diagnosed with scabies must be excluded from the childcare centre but it does not explain the time of exclusion. Please explain this in the PIS by reference to the Ministry of Health policies and the centre’s policies.
5. Please talk about the degree to which a child needs to be undressed (eg, can keep underwear on)
6. Please clarify for the Committee what your management steps will be should incidental findings occur.
7. Notifying GPs should not be optional.
8. The Consent form mixes up the use of “me” and “my child”. It should be “my child”.
9. The Committee noted a goal of the study is to see how common scabies is in New Zealand. The Committee felt that this would be difficult to do as this is a pilot study

Please be clear in PIS that as this is a pilot study and that this type of goal won’t be achievable at this stage.

1. Please remove the statement about pregnant partner from the Consent form.
2. The Committee questioned if parents would have to complete the questionnaire before they could be involved in the study.

The Researcher stated that they do not as they could still make a scabies diagnosis without this information.

Make this clear in the PIS and specify that there is a parental request in the questionnaire and that the rest is for “your child”.

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 Observation Studies, para 6.11*)
* Please provide age appropriate assent forms for children and consent forms for their parents/guardians (*Ethical Guidelines for Observation Studies,para 6.21*)
* Please provide evidence of favourable independent peer review of the study protocol (*Ethical Guidelines for Intervention Studies, Appendix 1*).
* Please ensure appropriately skilled staff administer the questionnaires (*Guidelines for Intervention Studies, paragraphs 5.36 – 5.37*)

This following information will be reviewed, and a final decision made on the application, by Dr Kate Parker & Ms Rochelle Style.

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| **6** | **Ethics ref:** | **18/NTA/129** |
|  | Title: | Latte dosage trial |
|  | Principal Investigator: | Dr Jane Alsweiler |
|  | Sponsor: | University of Auckland |
|  | Clock Start Date: | 09 August 2018 |

Dr Jane Alsweiler 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. Over 3,500 babies in New Zealand are born late preterm (34-36 weeks’ gestational age) every year, with a higher risk of long-term neurodevelopmental impairment than babies born at term.
2. Intermittent hypoxaemia (transient drops in oxygen saturation) is associated with neurodevelopmental impairment in preterm babies, and is common in babies born late preterm.
3. Caffeine is an effective treatment for intermittent hypoxaemia and improves long-term outcomes in babies born very preterm (< 32 weeks’ gestational age).
4. The most effective dose of caffeine to reduce intermittent hypoxaemia in late preterm babies has not been established.
5. This study proposes a randomised controlled trial to determine the most effective dose of caffeine to reduce the incidence of intermittent hypoxaemia in babies born late preterm.

Summary of ethical issues (resolved)

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

1. The Researcher stated the trial will be randomised and controlled into placebo (water) versus 4 different doses (5, 10, 15, 20mg/kg) caffeine. Participants will take their doses once/day in the morning until their reach term age.
2. The research team will look at baby’s intermittent hypoxaemia at Baseline, 2 weeks and term age and take saliva swabs from both mothers and babies to see what their caffeine levels are.
3. The Committee appreciated the quality of the Participant Information Sheet. It was nicely written and easy to follow. The Committee particularly liked the incidental findings policy. However, please add to the policy how you propose to handle incidental findings relating to safe sleeping issues and smoking.
4. The Committee queried if there would be follow up once the medicine was stopped.
5. The Researcher replied once stopped, the study would end. No follow ups would be made.
6. The Committee questioned if there would be high risk of withdrawal once babies come off caffeine.

The Researcher stated they have not seen withdrawals in the pre-terms.

1. The Committee suggested that it would be good to check on withdrawal symptoms and useful to collect this information.
2. .The Researcher confirmed that a Data Safety Monitoring Board (DSMB) has been established as a result of the peer review.
3. The Committee questioned why dosing could not be started low and progress to higher amounts with assessments being done in between.

The Researcher felt it would be harder to compare if they did not randomise and

because it is a small study, it would be hard to draw any conclusions on any interim analysis.

1. The Committee questioned if it would make a difference if the mother is drinking coffee.
2. The Researcher stated that they would conduct a caffeine intake questionnaire for mothers and hypothesised that intakes will change at different time points. The research team will take saliva samples from the mothers to adjust for caffeine levels transferred to baby during breastfeeding.
3. .The Committee questioned if breast milk could be used to test for caffeine.

The Researcher advised that due to practicality it is easier to use saliva testing instead. To get samples from breast milk there are a few things to overcome:

* Getting the mother to express her milk
* Some people do not believe in breast milk collection at the same time that mothers are using their milk for baby
  + Difficult to extract caffeine to measure once it’s absorbed in breast milk.

1. The Committee noted that late pre-terms are more susceptible to cerebral palsy and asked what is being done to inform parents of this.

The Researcher advised that there will be well trained health practitioners available to talk parents through this.

1. The Committee noted that peer review recommended not using a placebo and questioned the researcher on their thoughts on this.

The Researcher felt it was safer to have a placebo as 5mg alone might be a difference and that there would be no way to assess this.

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 include in your incidental findings policy how you propose to handle the incidental findings of safe sleeping and smoking

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

1. The Committee recommended that as swabs of saliva were being taken it would be good to confirm that they would not be used for genetic testing.
2. Please add side effects so parents are informed (eg, Irritability poor sleeping, possibly reflux)
3. Add that weight gain will be monitored.
4. Please apply the latest version of HDECs’ ACC statement (adapt where appropriate);

“If you were injured in this study, you would be eligible **to apply** for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery.  
If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.”

1. Please state that the study contributes to a PhD qualification.
2. The Committee noted that the consent form states that parent will be re-contacted. This needs to also be mentioned in the Participant Information Sheet.
3. Please use Ministry of Health ethnicity classifications when collecting ethnicity data to ensure the options available are suitable for New Zealand participants. These classifications are: New Zealand European, Maori, Samoan, Cook Islands Maori, Tongan, Niuean, Chinese, Indian, Other (such as Dutch, Japanese, Tokelauan) please state.
4. Please add that neurodevelopment outcomes may be looked at should baby undergo a significant change in intermittent hypoxaemia level.
5. Please state that diaries will need to be filled out daily.
6. Explain what the questionnaire is about in the PIS.
7. Please mention in the PIS what kind of incidental findings (eg, postnatal depression/cyanosis) might arise and how they will be dealt with.

Decision

This application was *approved* with non standard conditions.

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| **7** | **Ethics ref:** | **18/NTA/136** |
|  | Title: | Clinical Assessment of Gallus Mask |
|  | Principal Investigator: | Dr Robert Martynoga |
|  | Sponsor: | Fisher & Paykel Healthcare |
|  | Clock Start Date: | 09 August 2018 |

Dr Robert Martynoga (CI) was present by teleconference and Geoff Bold, Laurence Gulliver, Sean Craig, Paul Moody, Jane Loroma were present in person for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The study will undertake a clinical assessment of a new non-invasive ventilation mask. The mask will be placed on participants, and a questionnaire on how easy the mask was to set up and use will be completed by the bedside nurse at the end of each shift.

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 presence of the Gallus Mask and appreciated the demonstration.
2. The Committee questioned if there will be sufficient time in the consent process to consult with family if they are likely to be in the ICU/HDU setting.

The Researcher(s) stated that most patients will not be well enough to give consent, but if they are well enough the bedside nurse will go through the information sheet with them.

If participants are not well enough they will go onto standard care mask first or the research team will talk to relatives to get an idea of what the participant may want to do. The Committee suggested that a copy of participant information sheet be left with family members and a PIS be developed and uploaded for the Committee’s review.

1. The Committee questioned if health information collected will really be anonymous.

The Researcher(s) responded that there will be no personal data or demographic information collected.

1. The Researcher(s) confirmed that if participants withdraw from the study they will be put back on the standard of care mask.
2. The Researcher(s) apologised for not including the middle page of the cover letter.

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 provide a separate information sheet for nursing staff including what they are expected to do, what is being looked for, there is no coercion (ie staff won’t be paid) and it will not affect their employment if they do not wish to participate. A unique study number should be provided for the nurse participants to protect their privacy – names/initials should not be used. The Committee suggested that this will encourage honest feedback without pressure to provide good feedback. Please include in the nurses’ PIS the statement; “If we want further comment we would like to contact you. Please let us know whether this is acceptable to you or not.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

1. Please state that the mask has not been used on patients before and clarify, in relation to the statement that ‘all safety and performance testing has been completed’, that the testing is laboratory testing.
2. Please include an explanation in the PIS of the risks of using the mask. The PIS currently only states that the risks are the same as for other masks but the risks are not explained. Furthermore, it would appear that the risks may not be the same, at least insofar as pressure injuries are concerned.
3. Following on from the last point, a better explanation of the potential benefits of the mask would be helpful.
4. The Committee were curious as to why images were not allowed to be shown on social media.

The Researcher(s) explained that they had issues in previous trials, of photos with trialled masks released to the media.

The Committee asked that participants and relatives/persons interested are informed of this image ban on social media and the reason why. Please note this in PIS.

1. Please use HDEC’s most current template for commercially sponsored trials compensation (as found in the HDEC PIS template):

*As this research study is for the principal benefit of its commercial sponsor [insert name], if you are injured as a result of taking part in this study you* ***won’t*** *be eligible for compensation from ACC.*

*However, [insert name] has satisfied the [ insert name] Health and Disability Ethics Committee that approved this study that it has up-to-date insurance for providing participants with compensation if they are injured as a result of taking part in this study.*

*New Zealand ethical guidelines for intervention studies require compensation for injury to be at least ACC equivalent. Compensation should be appropriate to the nature, severity and persistence of your injury and should be no less than would be awarded for similar injuries by New Zealand’s ACC scheme.*

*Some sponsors voluntarily commit to providing compensation in accordance with guidelines that they have agreed between themselves, called the Medicines New Zealand Guidelines (Industry Guidelines).These are often referred to for information on compensation for commercial clinical trials. There are some important points to know about the Industry Guidelines:*

* *On their own they are not legally enforceable, and may not provide ACC equivalent compensation.*
* *There are limitations on when compensation is available, for example compensation may be available for more serious, enduring injuries, and not for temporary pain or discomfort or less serious or curable complaints.*
* *Unlike ACC, the guidelines do not provide compensation on a no-fault basis:*
* *The Sponsor may not accept the compensation claim if:*
* *Your injury was caused by the investigators, or;*
* *There was a deviation from the proposed research plan, or;*
* *Your injury was caused solely by you.*
* *The injury was caused by <<NAME OF COMPARATOR DRUG>> (include only if holds true for specific study)*

*An initial decision whether to compensate you would be made the by the sponsor and/or its insurers.*

*If they decide not to compensate you, you may be able to take action through the Courts for compensation, but it could be expensive and lengthy, and you might require legal representation. You would need to be able to show that your injury was caused by participation in the trial.*

*You are strongly advised to read the Industry Guidelines and ask questions if you are unsure about what they mean for you.*

*If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.*

1. Add that engineers will be making observations while the mask is being used. Please include what their functions will be during this time.
2. The Committee were happy with the best interest argument (Code of Rights, Right 7(4)) but this needs to be better articulated in the Participant Information Sheet (PIS), for example, by better describing the potential benefits of the mask such as reducing pressure injury to the nasal bridge and improved comfort.
3. Please also provide a better description of the mask in the PIS and how it is different to existing masks, for example, that it has an under the nose seal rather than an over the nose seal.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made 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 Karen Bartholomew & Ms Rochelle Style.

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| **8** | **Ethics ref:** | **18/NTA/130** |
|  | Title: | Safety, Tolerability, and Pharmacokinetics of AB-452 in Healthy Subjects and Subjects with Chronic HBV Infection |
|  | Principal Investigator: | Prof Edward Gane |
|  | Sponsor: | Novotech (New Zealand) Limited |
|  | Clock Start Date: | 09 August 2018 |

Professor Ed Gane (CI) and Olivia Thame 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.

Catherine Jackson declared a potential conflict of interest, and the Committee decided that she could leave the room and not take part in the discussion or decision making for this application.

Summary of Study

1. The study drug AB-452 is being developed as a potential new treatment for Chronic Hepatitis B virus infection (HBV).
2. This is the first clinical study where AB-452 will be given to humans.
3. The main goal of the study is to determine whether AB-452 is safe and well tolerated when given at different doses. The study will also measure the levels of the drug in the blood at different times and look at whether this is affected with or without food. It will also look at the interaction of AB-452 with another drug.
4. The study will be conducted in 2 parts. First part will be conducted on approximately 28 healthy people. Part 2 will be conducted on 48 patients who have chronic hepatitis B .

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 the trial to be a first in human. The research team planned to apply Single Ascending Dose (SAD) and Multiple Ascending Doses (MAD) in healthy volunteers then MAD in patients who have chronic HBV.
2. The Committee asked if this would be done in sequence or if they were going to report back at intervals and inform the Committee before going on to the next part.

The Researcher(s) responded that because it is an umbrella protocol, they would report back before moving into patients, ie, Part 2 of the research.

1. The Committee queried the process for moving from part 1 to part 2.
2. The Researcher(s) stated that Part 1 of the research involved two different stages. The First Stage of Part 1 is conducted using SAD in healthy volunteers. From that stage, a dose will be selected for MAD which is the Second Stage of Part 1 in healthy volunteers. Part 2 uses patients with Chronic HBV. The MAD in these patients will be based on one dose from the MAD in healthy from Part 1, stage 2. which will be the starting dose in patients and will continue ascending doses up to 3 dose levels.

They have an internal Safety Review Committee which Professor Gane is a part of. This Committee meets after each level of dosing to review safety before moving onto the next dose.

1. The Committee appreciated the use of the latest HDEC commercially sponsored trial compensation statement in the Participant Information Sheet (PIS).
2. The Committee questioned if $75 would be enough to cover parking costs.

The Researcher(s) explained that visits are short and this is sufficient for mileage and parking. They encourage participants to use taxis.

1. In relation to Part 2 of the research using patients, the Committee queried if there would be 4 cohorts, made up of 3 patient cohorts comprising those who are being treated for chronic HBV and 1 patient cohort comprising patients who have never been treated for chronic HBV..

The Researcher(s) stated that those on treatment will stay on treatment. Only once virus is completely eradicated will treatment stop. They predict that this will work within the 4 week period.

1. The Committee questioned if data would be sent overseas (eg, data attached to the analysis of samples).

The Researcher(s) replied that samples would be accompanied by a requisition form that would only have a participant’s unique subject number, gender and age on it. No data accompanying the samples will be identifiable.

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 there is very little information on risk so if unexpected side effects should come to light between each phase, please ensure both participants and HDECs are informed. Please do this before moving on to the next phase.
2. Please make it clear that it is first in human trial on the advertisement.

The Committee requested the following changes to the Participant Information Sheets and Consent Forms (where appropriate given the multiplicity of PISs (including the FUR PIS):

1. Please add the name and location of the overseas laboratory (ie, where in the US) that all samples (ie, optional blood samples as well) are being sent to.
2. Include a statement that where samples and data are being sent overseas that privacy protection may be different or less restrictive than in NZ.
3. –The study design description section is confusing. Please more clearly explain the different parts of the study and the different stages within each part - using a table may help to simplify the study methodology.
4. Please explain in lay term the line;”screening visit day minus 28, today minus 2” (page 4 of 18).
5. For the part 2 PIS, the phrase; “competitive enrolment” is used. Please change this wording to avoid the potential of pressuring patients into participation.
6. Please remove mention of genetic material in the relevant PISs (e “What could happen to me by giving these biological samples” section). The Researcher(s) confirmed that genetic testing will be done in patients but not in healthy participants, ie in Part 2 of the research and not in Part 1.
7. .Please make it clear that participants will not be able to get their samples back.
8. Explain what possible incidental/abnormal findings might be found and explain what action will be taken. This is mentioned in the consent form(s) but needs also to be included in the PISs.
9. Explain whether or not individual results are available and include a relevant section in the consent form(s)
10. Please include in the Pregnant Partner PIS rights of correction and withdrawal and if data is being sent overseas and, if so, what privacy protections will be in place. .

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*).

This following information will be reviewed, and a final decision made on the application, by Ms Toni Millar & Dr Brian Fergus.

|  |  |  |
| --- | --- | --- |
| **9** | **Ethics ref:** | **18/NTA/121** |
|  | Title: | Transcend Study |
|  | Principal Investigator: | Associate Professor Andrew Holden |
|  | Sponsor: | Surmodics, Inc |
|  | Clock Start Date: | 09 August 2018 |

Professor Andrew Holding (CI) and Miss Helen Knight were present in person for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This study aims to treat patients’ with Peripheral Artery Disease (PAD) using an angioplasty balloon which has been coated with a drug called ‘Paclitaxel’.
2. Drug Coated Balloons (DCB’s) have been shown to positively impact on re-narrowing within the treated artery.
3. The application of Paclitaxel to an angioplasty balloon has been well studied, with patients experiencing lesser rates of re-narrowing as the drug helps limit cell growth, specifically with scar tissue resulting from inflammation.
4. The challenge now with DCB’s, is to develop a device that ensures drug on the angioplasty balloon is delivered to the area of narrowed artery, and also the rapid transfer of drug into the artery once the balloon is inflated.
5. The study device, Surmodics SurVeil DCB has been designed with both of these challenges in mind, and with this clinical trial seeks further prove the effectiveness of the device.

Summary of ethical issues (resolved)

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

1. The Committee commended the research team on the Participant Information Sheet (PIS).
2. The Committee queried if tissue will be collected.

The Researcher(s) responded that bloods will be collected and will be kept at the hospital. No bloods will be sent overseas nor used for Future Unspecified Researcher.

1. The Committee noted the section on compensation (in PIS) does not use the full HDEC template wording. The Committee are willing to accept this now but please apply the full wording for all new applications to come.
2. The Committee questioned if participant data will be stored in folders.

The Researcher(s) stated that they would be stored in binders in their offices and, kept digitally.

The office is locked and access is by swipe cards x2. Upon study completion, the data will be archived and sent offsite to Penrose for storage. The electronic data will stored in Electronic Data Capture (EDC).

1. .The Committee indicated that the answer to question r.1.6 suggests that study will be halted if the sponsor deems it necessary. The Committee reminded the researchers that studies cannot be stopped simply for reasons of commercial interests or public relations.
2. The Researcher(s) confirmed that data would be de-identified rather than made anonymous. Please amend references to anonymity in the PIS.
3. The Committee noted that the peer review talks about double blind study design and questioned if surgeons can actually be blinded to the balloon used.

The Researcher(s) replied that surgeons will not be blinded to the balloon used and therefore the trial is single blind.

1. The Committee queried if it is necessary to include the contraception warning.

The Researcher(s) informed that on occasion (in past trials) pregnancy had occurred so felt it important to include as precaution.

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 talk to the sponsor about using New Zealand ethnicity categories for your

study documentation.

1. The Committee noted that the brochure refers to US Law, please change to New Zealand law or do not use the document.

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

1. Please clarify in the PIS that the device is seeking to improve drug delivery – this is not clear from the present explanation.
2. Please include information on the frequency of the side effects
3. Please clarify where in the United States the medical imaging is being sent and please note, in relation to the statement that participants’ information will be ‘handled in accordance with appropriate confidentiality standards and all applicable data protection land privacy laws” that these laws may be different to New Zealand law and may offer less protection.
4. For the Consent form, please ensure only statements that are truly optional have yes/no tick boxes next to them (ie, if participant ticks no, they can still take part). For example, is it optional for the images to be sent to Surmodics?
5. Please include a statement in the consent form in the section which refers to withdrawal that it is not possible to remove the stent.
6. Please explain that the Medtronic impact device is standard care.
7. Please explain in the PIS whether individual results will be available and whether incidental findings/abnormal findings might be expected (and if so, what they might be) and include sections in the consent form as appropriate.
8. Please be clear about the circumstances under which reimbursement payments will be made.

Decision

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

* Please apply New Zealand relevant categories and legislation. (*Ethical Guidelines for Intervention Studies, para 6.7(a)* )
* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).

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

## Review of approved studies

Ethics reference:17/NTA/12

Title: REMAP- CAP

Dr Colin MacArthur was present in person for the discussion of this existing study.

Summary:

* Currently conducting an HDEC approved study called REMAP-CAP. This has 4 sites in New Zealand and is just starting out in Australia. It has multiple arms and is a novel design. The interventional part of it is going fine but they want stronger recruitment.
* Dr MacArthur’s current concern is for those not eligible for the study.
* An online screening tool is used to screen for eligibility based on patient clinical characteristics.
* A patient either qualifies to be part of intervention study or does not.
* If they do not qualify then (i) they do not have disease of interest (Community Acquired Pneumonia-CAP) and nothing more is done with them or (ii) do have disease of interest but do not qualify for the intervention for whatever reason. The research team is only looking at one element of treatment (choice initial antibiotic) but in future will be adding other topical domains in areas of practice that will probably be examined in using the technique. At the moment a significant number of patients are being rejected from the intervention part of study because it is currently constrained and people have indications for specific antibiotics so study options do not apply to those patients.
* As part of overall design the research team feel it is important to understand whole population of patients that present to intensive care with CAP.
* The research team had originally proposed to seek additional information about non-intervention, non-randomised patients as part of observational data set and wanted to obtain additional information from patients not normally obtained and include respiratory secretion samples.
* HDECs current approval is based on consent from patients for both the observational and interventional parts of study.
* The research team now want to change what they would like to do with the observation cohort and the number of patients that might be involved.

Proposal:

The study has now been refined so its observation component is shrunk and conducted as an audit. It is using existing information with linkage to ICU registry showing basic data of ICU admission which is already being collecting as part of bench marking audit process and potentially linking with hospital discharge coding data. The data is collected and pulled together retrospectively. This is quite different from what they had envisaged and proposed, originally.

Summary of ethical issues (resolved)

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

1. The Committee questioned what will be done with the retrospective data.
2. The Researcher explained that it will be used to compare patients randomised with those not and to potentially modify the intervention part of the study to include more patients-to have it more comprehensive, change the current inclusion criteria but also to come up with new areas of treatment that will apply to the group that are currently excluded. In the future, the excluded group could become part of the intervention. The data will be used to improve the future study design. They may add new platform domains.
3. The Researcher confirmed the observational cohort will not be kept identified. They do not need to go back to this cohort at all.
4. The Researcher confirmed data is retrospective as the observation data is from clinical records and will be accessed post ICU discharge. The data linkage will be months later.
5. .The Committee wanted to know what concerns the other study sites had raised.
6. The Researcher informed the other sites were concerned that current HDEC approval requires consent from participants even though the study is not operating that domain yet and Dr MacArthur’s site is just seeking to identify participants that might enter the study. There is a difference in opinion as to whether, based on current HDEC approval, identifying participants that might enter the study would require consent.
7. The Researcher confirmed that the proposed change will operate as a retrospective audit and that eligible patients would be part of the intervention arm and those not eligible would be part of the screening log. Information obtained from patients would mostly not be sensitive nor identifiable. However, they would be using NHIs for linking.
8. Dr MacArthur questioned the Committee on its current approval and whether it covers identifying patients for the screening log without consent.
9. The Committee stated their view on the future question is; the study is taking a screen negative log and adding health information without consent which can be justified in this case for the purpose of scientific validity and public interest. The concern for the future question is if data is identifiable and/or sensitive.
10. It was agreed by the Committee and Dr MacArthur that it is usual practice and acceptable for patient information obtained for standard of care to be used in screening, without consent.
11. The Committee questioned if there are several groups of cohorts that the study would work with.

The Researcher explained that there are different domains but same patients. Patients in the registry arm would not be re-approached to be part of the study.

The Researcher confirmed that DHB legal team had reviewed their proposal in terms of

1. working out if patient qualifies or not
2. only seeking out those that qualify.
3. The research team still need to finalise what they want to do with the data in the screening log.

Decision:

1. The Committee clarified that what is essentially being asked today is, will consent be needed to keep a list of patients that fail screening?

The Researcher confirmed this and added that they would like to know if it is okay to hold names as potential registry only retrospective data collection without consent. The research team will only de-identify patient information once it is put in the screening log.

The Committee decided the current approval will remain unchanged which means the screening process will continue to not require consent.

## 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:** | 18 September 2018, 01:00 PM |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

The following members tendered apologies for this meeting.

* Dr Catherine Jackson
* Dr Christine Crooks

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 5.38pm