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| **Committee:** | Northern B Health and Disability Ethics Committee |
| **Meeting date:** | 07 March 2017 |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

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| **Time** | **Item of business** |
| 12.00pm | Welcome |
| 12.05pm | Confirmation of minutes of meeting of 07 February 2017 |
| 12.30pm | New applications (see over for details) |
|  | i 17/NTB/30  ii 17/NTB/31  iii 17/NTB/35  iv 17/NTB/36  v 17/NTB/37  vi 17/NTB/38  vii 17/NTB/39 |
| 3.45pm | General business:   * Noting section of agenda |
| 4.00pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Mrs Maliaga Erick | Lay (consumer/community perspectives) | 01/07/2015 | 01/07/2018 | Present |
| Mrs Stephanie Pollard | Non-lay (intervention studies) | 01/07/2015 | 01/07/2018 | Present |
| Miss Tangihaere Macfarlane | Lay (consumer/community perspectives) | 19/05/2014 | 19/05/2017 | Present |
| Mrs Phyllis Huitema | Lay (consumer/community perspectives) | 19/05/2014 | 19/05/2017 | Present |
| Mrs Kate O'Connor | Lay (ethical/moral reasoning) | 14/12/2015 | 14/12/2018 | Present |
| Dr Nora Lynch | Non-lay (health/disability service provision) | 24/07/2015 | 24/07/2018 | Present |
| Mrs Leesa Russell | Non-lay (intervention studies), Non-lay (observational studies) | 14/12/2015 | 14/12/2018 | Apologies |
| Mr John Hancock | Lay (the law) | 14/12/2015 | 14/12/2018 | Present |

## Welcome

The Chair opened the meeting at 12.00pm and welcomed Committee members, noting that apologies had been received from Mrs Leesa Russell.

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 07 February 2017 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **17/NTB/30** |
|  | Title: | Newton 2 - EG-01-1962-03: Comparison of EG-1962 to oral nimodipine in aSAH |
|  | Principal Investigator: | Dr Edward Mee |
|  | Sponsor: | Edge Therapeutics, Inc. |
|  | Clock Start Date: | 23 February 2017 |

Davina Macalister 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.

Mrs Stephanie Pollard declared a potential conflict of interest, and the Committee decided the conflict was not relevant and that Mrs Pollard could participate in the discussion and decision of the application.

Summary of Study

1. This is a multinational randomised trial of a new intraventricular (into a brain cavity) preparation of vasodilator nimipidine compared with the current standard care of oral, IV or IA nimopidine, in patients with subarachnoid haemorrhage less than 48 hours old.
2. A catheter as conduit to ventricles will already be in place for all to allow regulation of intracranial pressure.
3. All patients will have had a definitive procedure to plug the aneurysmal leak, surgically or by interventional radiology. Participants will be gravely ill and neurologically impaired but not so damaged that there is no real prospect of functional recovery. It is unlikely any will be able to consent at randomisation.
4. Clinical studies to date: Phase 1/2 study suggested the experimental treatment improves good outcome from 28% with current standard care (including oral nimopidine) to 60%.
5. This study: N=20 (NZ), March 2017-2018.Treatment: single 600mg intraventricular injection or oral preparation for up to 21 days (dose and duration may be varied as per standard care).
6. Matching placebos for each group
7. Primary outcome: efficacy as measured at day 90 by questionnaire
8. Secondary outcomes: many including Day 30 CT findings and health economic measures.
9. SCOTT approval received.

Summary of ethical issues (resolved)

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

1. The Committee noted that this application has been to CEN HDEC in 2016, was provisionally approved and then declined.
2. The Committee noted the need for enrolment without consent.
3. The Committee was persuaded by the arguments put forward regarding the ethics and legality of an independent physician assessment of "best interests". This is a serious condition with a high chance of severe long-term disability.
4. The Researcher(s) noted consent for follow up / pregnancy would be completed.
5. The standard care nimopidine is said to be a poor performer, though better than nothing. It also has some systemic side effects that may be avoided with a direct injection.
6. The Committee asked if data is used if someone passes away. The Researchers explained the sensitivity of talking to family in these cases, but noted there are many time points at which the data is important to be used in cases of death.
7. p.4.2 pg. 26: Maori cultural issues: Note guardianship aspect of tissue i.e. taking, storage and transportation. Applicants would do well not to refer to prayer (karakia) and access to Maori health services as being ‘something as simple as’.

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 participants will have 3xCT scans and asked what proportion of patients would have this number or more as part of standard care. The Committee also asked with regards to the MRA or angiogram at day 5-9. The Researcher(s) explained they would provide clarification on this in a cover letter, as well as update the Participant Information Sheet to clearly state what is involved in study participation.
2. There doesn't seem to be an assent PIS for relative/friend. Please create one and ensure the language used refers to the relative/friend.
3. The Researcher(s) explained recruitment process for these participants, relating to second parts of right 7(4) (family consultation). The Researcher(s) explained that they introduce themselves to family, explain why it was best to approach at the time they did, or why they think they should if not already enrolled, and talk to them while the research investigators will be talking to independent physician. Often the independent physician would be a critical care or emergency medicine doctor, for the second opinion.
4. The Researcher(s) confirmed they would remove the EPOA from the clinician consultancy form.
5. The Committee queried whether radiologist would be appropriate as an independent opinion. The Researcher(s) explained all neurosurgeons and anaesthetists would be involved in the study, so it means other clinicians must be consulted. The Committee requested it is a formal process rather than an ad-hoc process. I.e. add a pool of people who are aware of the study. It matters that the clinician is aware of the study as much as their clinical role.
6. The Researcher(s) explained the rotating meeting at which point there are opportunities to talk about the study.
7. Add detail in protocol on who is considered an independent physician and how this process works.
8. Provide information on socialisation of the research, for patients and for researchers.
9. The Committee asked how soon the participant could be asked whether they want to continue participation. The Researcher(s) stated could be weeks or months later. The Researcher(s) explained they check hourly, each day.
10. What occurs if someone does not want to be a part of the study? The Committee considered the data should be withdrawn in those cases. In addition if the participants was still in the phase of taking either oral nimodipine or matching placebo, it would require the blind be broken to determine whether continuing oral nimodipine was required as per standard care or whether the full course of nimidopine had already been given by intraventricular injection. .

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

PISC- Delayed consent

1. Semicolons populate this document in inappropriate places. Please revise
2. According to terms of attached SCOTT approval, GP notification is required. Go through PISCs and adjust to comply with this, removing advice for patient to inform GP and option of not having GP informed.
3. Under heading "Unforeseen Risks" read and revise the following sentence which doesn't make sense -' We do not know the effects of a lot of medicines on unborn children because EG-1962 is a new formulation...'
4. Remove reference to US law under "confidentiality"
5. Compensation from ACC not ACH!
6. Correct HDEC committee to NTB in PIS and on consent of all documents Pg 3 # 3. Highlight paragraphs 4 & 6 re reimbursement and medications to avoid during study.
7. Pg 6 'Compensation' para 1: Identify / clarify re courts mentioned here.
8. Pg 6 Contact details. Provide phone numbers, email addresses for Edward Mee, Davina McAllister and He Kamaka Waiora (Maori Cultural Support).

Decision

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

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

This following information will be reviewed, and a final decision made on the application, by Mrs Stephanie Pollard and Mrs Kate O’Connor.

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| **2** | **Ethics ref:** | **17/NTB/31** |
|  | Title: | eCoin for OAB |
|  | Principal Investigator: | Dr Sharon English |
|  | Sponsor: | Valencia Technologies Corp. |
|  | Clock Start Date: | 23 February 2017 |

Dr Sharon English and Miss Stacey Chambliss 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 an uncontrolled safety and efficacy study of an implanted tibial nerve stimulator (inside leg above ankle) for urge incontinence due to bladder overactivity.
2. There is quite good evidence (Cochrane meta analysis 2016) that direct tibial nerve stimulation (via a small needle through the skin, on a weekly sessional basis) is better than no treatment. The implanted stimulator will reduce the need for clinic attendances.
3. To date, the device has only been used in one human trial where 48 patients had a stimulator implanted into each forearm to treat high blood pressure.
4. There was a New Zealand site in the trial. There were 4 infections, 3/4 came from one Canadian centre.
5. This study:N=50 between New Zealand and USA. 2 New Zealand centres Recruited from clinic records.
6. Inclusion: Discontinue all bladder-active meds; >18 years, no upper age limit; severe symptoms of urge and incontinence refractory to behavioural and pharmaceutical standard care options
7. Exclusions: mainly relate to excluding other urinary tract pathologies, morbid obesity, peripheral neuropathy.
8. Intervention: local anaesthetic implantation of a 2cm diameter thin disc in subcutaneous tissue. Activated a month later.
9. Analyses/sample size: well described for a feasibility study.
10. DMSC: internal. No detail of who is to be on it. 10 visits over 12 months questionnaires 5 x 72 hour recording of detailed urinary history

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 they have not done testing to ensure no interference with pacemakers or other devices, as such this is an exclusion criteria. The Researcher(s) explained there is no lead wire so airport security is not an issue.

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 this is a first-in-human of the device in the leg and for this indication. This site is more likely to become infected than a forearm site yet there were 4/48 infections with the device in the arm. The exclusions do not include any consideration of poor arterial or venous circulation, chronic leg swelling (oedema) or diabetes all of which will increase infection risk. Infections in this site can lead to chronic ulceration. The Researcher(s) explained that this is a clinical decision, if someone had poor skin or something that would exclude them the clinician would not enrol them.
2. The Committee noted a Professor in Urology has provided the peer review from a reputable USA institution. He claims no conflict of interest but discloses he was involved with Valencia in the design of the study. Further local peer review is required from a urologist. The Committee would also like it sent to a local vascular surgeon for his/her review of whether the exclusion criteria are sufficiently comprehensive- should those with peripheral vascular disease, diabetes, chronic lower leg oedema, local skin disease on the lower leg be specifically excluded.
3. There is also no consideration of possible physical trauma from contact sport or footwear such as boots, which potentially press on this area.
4. Issues around compensation for injury. According to the applicant's answer to r.1.7.1.2, this research is not being done primarily for the sponsor. The Researcher(s) confirmed that it is for the sponsor.
5. Please submit evidence of sponsor insurance.
6. On the Participant Information Sheet , the compensation statement says two things at the same time, stating both that you are not/ you are eligible to apply for ACC. There is no evidence of sponsor indemnity provided, just an agreement between the sponsor and one of the two sites about indemnifying the investigator. The Committee requested that the sponsor must therefore show the committee evidence of adequate insurance and write the Participant Information Sheet to reflect this.
7. R.1.6 pg 14: States that ‘the study can be terminated at any time for any reason’. The Committee noted purely commercial reasons are not acceptable.
8. Revise American wording on the participant brochure.

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

1. American spelling – revise.
2. No number pages (? Nic my copy had page numbers NL). Suggest use HDEC template.
3. Device Removal: Clarify re cost if any, to have device-removed at/after the 12 month monitoring visit.
4. What if something goes wrong. Explain what and where the 'courts' are that are referred to in statement 'You would be able to take action through the courts'. Confidentiality: Explain ‘authorised representatives’ or their ‘designee’. Also explain ‘regulatory bodies’. Add: Maori Health Support details (as separate and distinct from HDC).
5. Please explain the words "diathermy", "electrocautery"
6. The PIS is deficient in providing any information about this being a first use of the device for the indication of overactive bladder, or that it has only been implanted in 48 people to data for any indication. The list of side effects and percentage risk implies a history of use of the device in humans which does not exist.
7. Pg.7 "The study sponsor will pay for the device to be removed if required due to research-related injuries". Please explain why the sponsor is limiting their responsibility in this way as the statement before this implies the sponsor will cover removal costs regardless of reason. The Researcher(s) acknowledged this was not well worded and would ensure it was consistent with other statements in the Participant Information Sheet.
8. Need to inform within the PIS,what will happen to all data collected up to the time of a premature withdrawal of consent.
9. Study Contact: replace the USA doctor contact with local PI Provide a Maori contact, not just the generic HDC contact
10. Consent form: Remove tick boxes from mandatory clauses, noting that GP notification should not be optional, and within the PIS, is mandated Modify pregnancy statement to fit this project. There is no risk to the pregnant partner of a participant. Remove clause describing sending tissue overseas - not part of study.
11. Implantation card: Improve the clarity regarding prohibition of MRI. Medical personnel would, not in New Zealand necessarily immediately understand a circle containing the letters MR with a line through it.

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Please provide evidence of favourable independent peer review of the study protocol (*Ethical Guidelines for Intervention Studies* Appendix 1).
* Please submit evidence of sponsor insurance. *(Ethical Guidelines for Intervention Studies para 8.4).*

This following information will be reviewed, and a final decision made on the application, by Dr Nora Lynch and Mrs Phyllis Huitema.

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| **3** | **Ethics ref:** | **17/NTB/35** |
|  | Title: | A Study to Determine Potential Drug Interactions with ACH-0144471 in Healthy Subjects |
|  | Principal Investigator: | Dr Paul Hamilton |
|  | Sponsor: | CNS |
|  | Clock Start Date: | 23 February 2017 |

Dr Paul Hamilton and Mrs Ellis-Pegler 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 study looking for potential effects on the pharmacokinetics of ACH-0144471 (a novel complement factor D inhibitor) from 3 drugs which are each metabolised through different pathways, and vice versa- the effects of ACH-0122271 on pharmacokinetics of each of the three representative drugs. Subjects are healthy adults 18-60, male and non-conceiving women. There are 3 separate studies within the protocol and each will involve a separate cohort of ~12 participants.
2. Each study involves giving a single dose of the potentially interacting drug (midazolam, fexofenadine or mycophenolate mofetil) and measuring its pharmacokinetics. After a 3 day wash out, the single dose of the same drug is given again against a background of ingesting ACH-014471 for 4 days. Further pharmacokinetic bloods are taken over several days.
3. Total inpatient stay days ~10 Time in study from screening: up to 50 days Peer review: via SCOTT.

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 explanation about the study from the researcher was much clear than the Participant Information Sheet.
2. Please consider a table for visits to reduce length.
3. The Committee noted ACS often submitted Participant Information Sheet with tables.

Summary of ethical issues (outstanding)

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

1. b.4.5 pg 13 States that tissue will not be made available for FUR yet consent form seeks for it to be used in 'additional non genetic complement system testing'. Please explain.
2. p.4.3.1 Provide update re Maori consultation. Mrs Helen Wihongi has reviewed.
3. Please explain how safety is monitored from an ongoing basis. The Researcher(s) stated with single doses and significant period of washout safety monitoring would be between sponsor and PI. Please make the process clearer for intervals for internal monitoring. Provide a monitoring plan.

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

1. The Committee noted inclusion and exclusion criteria is long. F.2.1 of application gives more condensed version, for example. Have general exclusions too – for example say that the Dr will review, to avoid emotive language being used in the document.
2. Exclusion criteria pg 3. Self identification of issues? e.g. mentally, legally incapacitated, significant emotional problems'. Make this clear or remove it.
3. The Committee explained tables could resemble the protocol schedule of events, but in lay language.
4. Please address co-administered drug side effects.
5. Make any restrictions on driving clear.
6. Page 5 - Samples used for non-genetic testing after study, is this future unspecified research? If it refers to FUR outside this study, it requires separate PIS and Consent Form.The Researcher(s) stated they will seek sponsor views on this.
7. The Committee queried whether drug of abuse findings would be sent to the GP. The Researcher(s) stated they do not. The Committee queried whether they would notify the GP of any medical incidental findings? The Researcher(s) stated yes. The Committee requested that this should be clear, what would and would not be sent to GP. The Committee queried whether they would contact a participant prior to informing GP. The Researcher(s) stated yes they would discuss with the participant.
8. Add review by NTB HDEC and reference to advertisement.
9. pg 11. What will happen to my test samples; para 3. Explain 'partner laboratory' Explain that it will be sent overseas (refer r.3.7 of appln - pg 18) and where.
10. pg 14 Potential costs / reimbursements: para 2. Clarify re whether that means $8000 in total. para 3: Statement re deductions from final study payment could be deemed inappropriate and open to abuse of participant rights. Reconsideration and rewrite of this would be advisable.
11. Please remove the need to withdraw in writing.
12. pg 16 1st paragraph. Does not make sense as it currently stands. Replace 2nd ACC reference with ACS? Also identify which 'courts' being mentioned here. pg 16 2nd last para: Somewhat vague. Suggest rewrite this statement with more specificity.
13. Consent form (pg 19): Identify 'regulatory agencies' that may access participant medical records. Identify who 'they' are with respect compensation payment.
14. Exclusions: what does "regular alcohol consumption within 6 months of screening visit" mean. Perhaps clarify or remove.
15. The Researcher(s) confirmed people have access to phones.
16. Confirm that storing specimens for up to a year after the study is for future testing in relation to this trial.
17. Char broiled (explain in New Zealand language). Page 5.
18. Add ‘carry the participant card’ to responsibilities.
19. Consent form – page 19 – what does this tissue testing refer to? Clarify whether this is unspecified, and if so, then future unspecified.

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Please clarify future unspecified research.

This following information will be reviewed, and a final decision made on the application, by Mrs Stephanie Pollard and Mrs Mali Erik.

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| **4** | **Ethics ref:** | **17/NTB/36** |
|  | Title: | A Phase 1b study to evaluate safety and tolerability of GS-9688 in Patients with Chronic Hepatitis B |
|  | Principal Investigator: | Prof Edward Gane |
|  | Sponsor: | Gilead Sciences, Australia & New Zealand |
|  | Clock Start Date: | 23 February 2017 |

Prof Edward Gane and Ms Oliva Thame and Ms Yung Chen 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 1b randomised controlled trial of a new acting antiviral (GS-9688) against hepatitis B in patients with chronic hepatitis B.
2. The first-in-human Phase 1a trial in healthy volunteers is ongoing; as of Feb 2017, 24/102 participants had completed at doses of either 0.5mg or 1.5 mg.
3. Study outcomes: safety, efficacy, pharmacokinetics, pharmacodynamics 2 optional substudies with separate PISCs: Genomic research and FUR to 15 years.
4. The study is in 2 parts and involves ~40 participants.

Summary of ethical issues (resolved)

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

1. The Researcher(s) explained that in the 1a study there had been 50 dosed as of last weekend. The last set have been fasted and fed in an ascending dose fashion.
2. The Committee asked why there is not a sequential programme (1a to 1b/2a etc), rather than being done in tandem. The Researcher(s) explained that we have completed the first phase. There will not be any further cohorts, and all relevant data is informing the current study. The Committee thanked the researcher for this explanation.

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 participants are referred from hospitals around the country. The Committee noted that the SCOTT approval requires GP being informed – please ensure SCOTTs requirements are followed and any changes are explicit, for instance if GP notification is mandatory.

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

Participant Information Sheet:

1. Table 1- explain QW
2. Why does the main PIS contain the statement that samples may be stored at the end of the study for up to 15 years? This is unnecessary and belongs in the Optional FUR PISC.
3. Page 6-7 – please revise terms, TLR8 SNP test for instance.
4. Page 4 – ‘return of drug’ please remove.
5. Pg 1, bullet pt 1. Explain 'genomics' (as done in Optional Genomic Substudy consent form).
6. Pg 2, paragraph 1: 'Regulatory authorities' - who are they and where?
7. Pg 2, 2nd last bullet pt: Explain 'cohort' here rather than at pg 3.
8. Pg 9: Explain 'HBV-DNA'. Please explain.
9. Pg 11: Re 'What samples will be stored etc' - First sentence appears not to make sense. Same paragraph: Define 'another country' i.e. say where.
10. Pg 13 Suggest change statement 'Total abstinence from intercourse is acceptable' to 'Total abstinence from intercourse is an acceptable birth control method'.
11. Pg 14: Last paragraph regarding possible benefits: Statement ' Your taking part in this study may help people etc' seems out of context. Suggest delete.
12. Pg 15, paragraph 3: Statement 'Your participation in this study may be stopped at any time by your study doctor, Gilead Sciences Inc or regulatory authorities' Further explanation required including re regulatory authorities.
13. 2nd last para: Concern re statement: 'any additional travel costs will be deducted from your final study payment'.
14. Pg 16, paragraph 2: re early withdrawal including if found ineligible, what arrangement to compensate for costs incurred e.g. travel. Please add ‘payment for reasonable travel expenses incurred’.
15. Paragraph 3: What and where are the 'courts' being referred to in statement 'You would be able to take action through the courts'. Please make this relevant to a New Zealand context.
16. Page 17, para that begins ' In accordance with relevant New Zealand privacy etc. is confusing to say the least. Suggest re-write. Please instead have a caveat about withdrawal if they violated the blind by accessing records, but noted that participants maintain the right to correct their records at any time .
17. Statement: 'Please contact study team member named at the end of this document'. Add details re contact person.
18. Add examples of ‘relevant authorities’ regarding access to records.
19. Add extn # for Prof Gane and/or mobile # and 0800 # as per Optional Genomic Substudy consent form.
20. Divide contact details – who to contact for what etc.
21. Please make it clear that the study drug is not available post study.

Participant Information Sheet FUR:

1. Same comments as above regarding Prof Gane's contact details.
2. p.4.3.1 pg 25: Provide update re Maori consultation. The Researcher(s) stated it is underway.

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 Mrs Stephanie Pollard and Miss Tangihaere. Macfarlane

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| **5** | **Ethics ref:** | **17/NTB/37** |
|  | Title: | The Benzathine Penicillin G Pharmacokinetics Study |
|  | Principal Investigator: | Dr Dianne Sika-Paotonu |
|  | Sponsor: | Victoria University of Wellington |
|  | Clock Start Date: | 23 February 2017 |

Dr Dianne Sika-Paotonu and Dr Ramona Teitei 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 study explores the pharmacokinetics of benzathine penicillin by monthly injection in children and young adults receiving secondary prevention of Group A streptococcal infection following rheumatic fever. It is noted that this is an old therapy and that there is little PK data derived from the sort of child populations where it is being used for this indication. There is an aspiration to eventually use the pk data to produce a more durable, less painful and more effective prophylaxis.
2. Design: Recruitment target N=50 ( need minimum of 25) between July 2017-July 2019 Wellington area
3. Recruiting procedure: public health nurse with whom they have an ongoing therapeutic interaction, asks permission for the research nurse to make contact, explain and consent.
4. Whats involved: in study for 6 months, baseline venous blood test finger prick sampling x7 over a month, then a few other random samples (up to total of 16) over a 6 month period. Throat swabs x 6 over 6 months Blood samples sent to Australia for processing. Throat swabs to Wellington lab.

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 if the researchers have any link to a pharmaceutical company who may take your work and use it to develop a new product. The Researcher(s) stated there are some links. The Committee requested this is clear in the Participant Information Sheet.
2. Clarify how you decide when to take finger prick samples apart from the 7 done over a month period and how many. The Researcher(s) stated 12. The additional 4 are obtained if there is a breakout infection or to fill in gaps for time points missed during the intensive month of sampling. The Researcher(s) explained the rationale behind when pricks are taken.
3. The Committee noted there might be issues with PK data analysis relating to the samples being taken in relation to different monthly injections rather than all taken sequentially over a single month. The Researcher(s) acknowledged the limitation.
4. Please explain how you will use the pain scale for the 5-7 year olds, noting it looks like an adult-observed tool suitable for acute pain but not useful to estimate pain from an injection given days or weeks ago. The Researcher(s) stated it related to pain at time of injection, another study looks at pain over time. This study looks at acute pain.
5. The Committee noted the locality is not participant’s homes rather it is the DHB.
6. The Researcher(s) explained the peer review that has occurred for the study. The Researcher(s) confirmed study is same as Australian study except for recording BMI.

Summary of ethical issues (outstanding)

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

1. The Committee noted the record forms for baseline and the 7x monthly contact visits show you are collecting extensive information about skin disease of participants including checking the entire body for sores, nits, scabies and tinea, and also taking swabs from skin lesions. Yet nowhere in the protocol or any of the Participant Information Sheet forms is there mention of anything other than throat swabs. Justify this. The Researcher(s) acknowledged that assessment was correct. Add to protocol and Participant Information Sheet.
2. How will results from skin or throat which show streptococcal infection, be acted on?
3. Both the parental and the young persons (11- 16 years) offer $30 koha but HDEC form says only $30 in total. The Committee think it would be fairest to offer something to both parties.
4. Take into account age- appropriate koha and explain what will be given to participants to the HDEC.

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

PISC - parent/guardian (many of these comments may be extrapolated to the other).

1. Add Maori cultural statement.
2. Add What is happening to human tissue. Indicate that the blood samples go offshore, give address of where to be held and processed. Not clear where testing will occur, by whom
3. Add compensation statement.
4. Pg2 The statement "The BPG injections used today to prevent ARF in children and adults are based on these old tests". This statement has the potential to undermine confidence in standard care treatment and is best removed.
5. Pg 2 "Why is my child being asked to participate?" Rewrite this in the 3rd person. Currently it places the reader as the participant.
6. The 4 options to which participants may consent separately, needs an 'and/or' instead of just 'and'. Can you really be in the study if you don’t consent to blood samples?
7. Pg 3 Consent to store samples for 5 years. Providing this refers to doing new tests on the samples which is still part of this same study (eg a different way of measuring penicillin level) then The Committee is satisfied the study is ethical without a separate FUR document. The applicants answer to b.4.5 - no storage in a tissue bank- implies this is the case. Make it clearer in the Participant Information Sheet that this is so.
8. Pg 3 "Risks etc" be specific about the number of finger prick tests, mention where the appointments will occur (? home)
9. Include somewhere in the PIS, the following information; - that pain questionnaires will be completed - right to withdraw consent part way through
10. Contacts: Give phone numbers not just emails for PIS. Provide Maori and Pasifica contacts independent form the project.
11. Consent form: The following terms need explanation or deletion: "retrospective"," prospective", "positive isolates" The Committee would prefer to see the whole HDEC template used,( with the non-relevant items such as the Pregnancy statement removed ).Particularly the statement that the opportunity to discuss with whanau etc has been provided.
12. Can you really be in the study if you don't consent to blood samples, data collection and the day 21 visit? Please clarify, currently unclear.

Pictorial assent document (Suitable for 5-11 year olds)

1. In 3rd speech bubble, a critical word is missing. Currently reads "We work in a medical school and we want to you and other young people living with ARF"
2. Include number of finger prick tests which will occur
3. Remove reference to participation reducing pain of injections for them. Unlikely to benefit individually in the near future ("We need your help in this study to make a better BPG medicine for you so it won't hurt as much and can last longer")
4. Add a signing/marking panel for child Assent 11-16 years.Remove or explain "deidentified" on consent form
5. Why does assent form say "We/I give our/my permission... " ?

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Please provide age appropriate information sheets and assent forms for younger participants and amend the existing information sheets and assent/consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).

This following information will be reviewed, and a final decision made on the application, by Dr Nora Lynch and Mr John Hancock.

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| **6** | **Ethics ref:** | **17/NTB/38** |
|  | Title: | Comparison of the blood levels of two forms of ferrous sulfate/ascorbic acid in healthy male volunteers under fasting conditions with diet control |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Ferromedica Pty Limited |
|  | Clock Start Date: | 23 February 2017 |

Dr Noelyn Hung, Dr Tak Hung and Linda Folland was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This is a Phase 1 bioequivalence study of an iron/vitamin C tablet (Ferromedica) compared with a reference product (Abbott) for iron pharmacokinetics. N=24 males 18-55 years
2. Design: Cross-over 2 period random sequence, 1 week washout between periods Intervention: a single tablet (325mg iron/500mg vit c) in each period Duration of inhouse residence: 36 hours each period. Diet restrictions: dosed after 12 hour fast, have to eat meals provided by the research centre for 4 days before each dosing weekend (?an added benefit for hungry Dunedin students) Total blood take ~160ml Study finishes with a followup phone call 7 days after last dose Recruitment: from centre database and with website advertisements which have been provided to committee
3. Peer review provided
4. Evidence of insurance provided.
5. Internal DMC- appropriate

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

1. Pg 6 If participants withdrawn for medical reasons by the investigator, why are they only reimbursed prorata? The Researcher(s) confirmed this is an error.
2. Statement pg 9 regarding providing ethnicity and A/E data to local rununga, best put higher up in document, not among contacts.
3. The Committee stated compensation statement contained a good level of detail.
4. The Committee noted participants have the right to access and correct data about them.

Decision

This application was *approved* by consensus.

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| **7** | **Ethics ref:** | **17/NTB/39** |
|  | Title: | The effect of 1,3-butanediol on immunity in athletes |
|  | Principal Investigator: | Mr David Shaw |
|  | Sponsor: | Auckland University of Technology |
|  | Clock Start Date: | 23 February 2017 |

Mr David Shaw 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. A PhD candidate study investigating the effects of a food additive (1,3,butanediol) which induces mild ketosis, on the immune functions (as measured in blood and saliva) and also on performance, of ~18 regular endurance athletes cycling flat out in a sports laboratory for 120min.
2. The reason for doing this is that athletes are already using this supplement to boost performance but there is inadequate information about its effects on the immune system (which can be compromised by high endurance sport).
3. A pilot study preceding the main study, will allow determination of the optimal dose of 1,3 butanediol.
4. Design: randomised placebo-controlled crossover.
5. Note: Submitting an ethics form from an academic institution in lieu of submitting a formal a protocol (thus requiring this committee to pick through to find the relevant bits) is disrespectful.

Summary of ethical issues (resolved)

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

1. The Committee queried whether doses are based on recommended safety data. The Researcher(s) stated compound that is connected to another similar ketone informed this studies dosing.
2. Please explain the data safety monitoring arrangements. The Researcher(s) stated the CI and supervisors would make the call if someone needed to be withdrawn. The Researcher(s) confirmed they would not be blinded.
3. The Committee noted the university owns IP generated from the PhD, though the student can copyright the thesis.
4. The Researcher(s) explained consent process.

Summary of ethical issues (outstanding)

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

1. Security of personal data See r.2.1.1. The Committee asked for more information on confidentiality, noting the reliance on "private use computer". The Researcher(s) explained the confidentiality measures. The Committee noted it would be safer to use a password protected PC located at AUT, and to use the cloud system from AUT for storage. Please add this detail to the protocol.
2. Add healthy males to the title of the study, as this is an important feature of the research.
3. The Committee asked whether this study falls under a trial involving a new medicine, as other supplements provided in high doses or for therapeutic indications had required SCOTT review in the past. The Researcher(s) stated they had checked with Medsafe. The Committee requested evidence of this.
4. The Committee requested the researcher add stopping rules for the study.
5. The Committee asked about identifiably of data. The Researcher(s) explained data would be de-identified at the end. For a period some level of identifier will be on a personal computer. The Committee stated a link could be created so data is linked without personal identifiers on the main-use data set. Similarly for questionnaires this should use a study number. Please view the National Ethics Advisory Committee Guidelines on Intervention Studies for guidance on levels of identifiably. Data should be coded to balance protection of information with the ability to re-link for safety reasons.
6. The Committee requested that a protocol is created and submitted rather than the AUT application form.
7. The Committee asked what the process was in the event of incidental findings. The Researcher(s) stated they would let the participant know. The Researcher(s) stated they do not have the clinical expertise know. The Committee noted there is a need to have someone review the laboratory results, which could lead to a referral to their GP. This person could be part of the data safety monitoring review.
8. Revised answer re p.4.3.1 (Maori consultation) misses the mark. The requirement to consult is on the applicant not the study participant. Please explain the consultation plan, but note the actual consultation can happen after you submit to ethics. The Committee Suggest consultation with AUT kaumatua council / He Kamaka Waiora.
9. Submit advertising wording for social media.

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

1. The Researcher(s) confirmed they would not provide the product to participants after the study. The Committee noted this should be clearly stated in the Participant Information Sheet.
2. The Participant Information Sheet needs to be changed to include HDEC/NTB as authorising body, provide appropriate Maori and HDEC contacts.
3. The Committee noted the Participant Information Sheet is rather too enthusiastic about the benefits of the research to individuals partaking. Combined with the "free dietary assessment worth $250" from the researcher, there is definitely an element of coercion here, which will need to be toned down. Remove to the section ‘will I be paid to be in the study’ and remove the dollar value.
4. The Researcher(s) explained they were doing the study to understand the safety of the intervention rather than prove it is helpful for athletes. The Committee noted this is a good scientific question and should form the rationale for the study, and this should come across in the Participant Information Sheet.
5. The Researcher(s) confirmed they would clearly discuss with potential participants that the product being used is not batch tested, so there is risk of incidental contamination with a banned substance.
6. Convert the Participant Information Sheet to the HDEC template. This will assist with including all relevant information for participants. Please also view the HDEC informed consent checklist found at <http://ethics.health.govt.nz/> under quick links.
7. Add information about blinding, study design.
8. Reword section stating ‘must be prepared to have human body measurements’, to remove mention of religion or culture.
9. Add section to consent signing panel to check off that the investigator has discussed the study with the participant.
10. Costs of Participating: Pg 2: Statement is contradictory: Starts: ‘There is no financial commitment, then goes on to say ‘participants will be required to pay for their own food and commit about 23 hours to the study.
11. The Committee noted the potential need to travel to/from Mairangi Bay, explain reimbursement for participants.

Decision

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

* Provide further information on the study design, *in particular the aspects outlined in the ‘outstanding ethical issues’, in a new protocol* (*Ethical Guidelines for Intervention Studies para* 5.4)
* Please provide criteria for study termination. (*Ethical Guidelines for Intervention Studies* *para 6.64*).
* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Please see (*Ethical Guidelines for Intervention Studies para* 7.2) for more information on levels of data confidentiality.
* Submit advertising wording.

This following information will be reviewed, and a final decision made on the application, by Mrs Stephanie Pollard and Mrs Kate O’Connor.

## 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:

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| --- | --- |
| **Meeting date:** | 04 April 2017, 12:00 PM |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

1. **Problem with Last Minutes**

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

The meeting closed at 3.50pm