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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 18 December 2015 |
| **Meeting venue:** | Via Teleconference |

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| **Time** | **Item of business** |
| 12.00pm | Welcome |
|  | New applications (see over for details) |
|  | i 15/NTA/210  ii 15/NTA/211  iii 15/NTA/212  iv 15/NTA/213  v 15/NTA/214  vi 15/NTA/215  vii 15/NTA/216  viii 15/NTA/217  ix 15/NTA/219 |
| 4.00pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Brian Fergus | Lay (consumer/community perspectives) | 01/07/2015 | 01/07/2018 | Present |
| Ms Raewyn Idoine | Lay (consumer/community perspectives) | STH CO OPT | STH CO OPT | Present |
| Ms Mali Erik | Lay (consumer/community perspectives) | NTB CO OPT | NTB CO OPT | Present |
| Miss Tangihaere Macfarlane | Lay (consumer/community perspectives) | NTB CO OPT | NTB CO OPT | Present |
| Dr Patries Herst | Non Lay (intervention studies) | CEN CO OPT | CEN CO OPT | Present |
| Dr Nicola Swain | Non Lay (intervention studies) | STH CO OPT | STH CO OPT | Present |
| Dr Nora Lynch | Non Lay (intervention studies) | NTB CO OPT | NTB CO OPT | Present |
| Dr Charis Brown | Non Lay (intervention studies) | 11/11/2015 | 11/11/2018 | Present |

## Welcome

The Chair opened the meeting at 12.00pm and welcomed Committee members.

The Chair noted that fewer than five appointed members of the Committee were present, and that it would be necessary to co-opt members of other HDECs in accordance with the SOPs. Ms Raewyn Idoine, Ms Mali Erik, Miss Tangihaere Macfarlane, Dr Patries Herst, Dr Nicola Swain, Dr Nora Lynch confirmed their eligibility, and were co-opted by the Chair as members of the Committee for the duration of the meeting.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

## New applications

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| **1** | **Ethics ref:** | **15/NTA/210** |
|  | Title: | Enhancing Engagement in a Stopping Violence Programme |
|  | Principal Investigator: | Dr Eileen Britt |
|  | Sponsor: |  |
|  | Clock Start Date: | 14 January 2016 |

Dr Eileen Brit was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The study assesses whether two short motivational interviewing sessions delivered before a stopping violence programme increases the effectiveness and engagement in the programme. Currently engagement is low.
2. The Committee noted that the flow diagram was helpful.

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 there will be participants who have poor literacy. The Researcher(s) explained that there are stages of the process prior to consent where the staff from He Waka Tapu will evaluate whether it is appropriate for someone to participate or not, which includes gauging literacy. There are verbal discussions that support the written information.
2. The Researcher(s) confirmed it was computer randomisation.
3. The Committee queried whether the researchers were satisfied that the quality and integrity of the motivational interviewing could be effectively quality assured, noting that there were 20 participants, 3 deliverers and the quality control will assess 5 interviews. The Researcher(s) acknowledged that this sample size was insufficient and will increase the number of quality assurance checks by the independent reviewer.
4. The Committee queried whether all participants would be Maori. The Researcher(s) stated many would be, but as He Waka Tapu refers anyone from the courts on request there could be Pasifika and Pakeha.
5. The Researcher(s) confirmed there would be interpreters.

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 requested that exclusion criteria are added to the protocol. Please also add the verbal support in the informed consent process, noting the potential for low literacy and need for support.
2. (Questionnaire). To ensure the questions on stopping violence are distinguished from the stopping violence programme please consider bolding.

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

1. Add a customised footer.
2. Incorporate bullet points to help with the readability of the document. Consider use of white space.
3. Add information indicating that there are interpreters available.
4. Add Maori support contact details.

Decision

This application was *approved* by consensus.

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| **2** | **Ethics ref:** | **15/NTA/211** |
|  | Title: | COMMENCE TRIAL |
|  | Principal Investigator: | Mr Adam El-Gamel |
|  | Sponsor: | Edwards Lifesciences |
|  | Clock Start Date: | 14 January 2016 |

Ms Kristy Abercrombie, Ms Liz Low and Dr Adam El-Gamel 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. Multi-national trial that aims to confirm that changes to the tissue processing, valve sterilization and packaging of the study device maintain the devices safety and effectiveness.
2. The Committee noted that the aortic valve arm is full. This application is only for the mitral valve.
3. The Researcher(s) explained that the valve is in common use. No changes to the implantation technique – only change is how the valve is prepared. The changes aim to increase the longevity of the valve.

Summary of ethical issues (resolved)

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

1. The study will be stopped if the failure rate or issue rate goes beyond the existing rate for the current values (which is roughly 15-20% for long term failure) Failure or issues can take up to 10 years to show up. However it such issues were occurring within the first 2 years of implantation we would stop the study. The rate of failure in the first year is very low, and usually is due to infection. The 1-2 year rate around 1%.
2. The Researcher(s) confirmed Maori consultation had completed.

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 stated that the study would meet the criteria for ‘use of human tissue’, due to the possibility of blood being sent overseas if a device were removed. The Researcher(s) confirmed that any device that had to be removed was mandated to be sent back to the sponsor.
2. The Committee noted insurance is for 30 per site however the application states 50. The Researcher(s) stated they would increase insurance if they experience high levels of recruitment.

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

1. The Committee requested that information on the potential for blood to be sent overseas be added to PIS. Include information on storage, destruction etc.
2. The Committee requested a review of the document for lay language, in particular the purpose of the study.
3. Be consistent with abbreviations TOE and TEE.
4. The Committee noted that participants can withdraw from the study verbally, rather than in writing (page 9). While a written withdraw can be an option, participants always have the choice of verbally withdrawing, and this should be made clear to participants.
5. Page 9 states ‘as per information above’ however there is no information above. Might be a copy pasting issue.
6. Add lay language title.
7. Add extension number for Maori contact details.
8. Review document for repetition.

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 the Secretariat.

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| **3** | **Ethics ref:** | **15/NTA/212** |
|  | Title: | To Investigate the Efficacy and Safety of Mongersen for the Treatment of Subjects with Active Crohn's Disease. |
|  | Principal Investigator: | Dr James Brooker |
|  | Sponsor: | celgene Pty Ltd |
|  | Clock Start Date: | 14 January 2016 |

Dr James Brooker and Ms Nancy Carey were not 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. R.2.5 ‘outlined in the clinical trial agreement’. In future applications please include this information in the form rather than referring to the CTA.
2. A Phase 1 study to test the effects of a new medication to find out whether or not it can or cannot improve the symptoms of Crohn’s disease
3. 1064 participants worldwide, randomised into 4 arms

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 the study should not be halted for commercial reasons.
2. The Committee asked that it is clearly indicated that the biomarker testing in this study is mandatory. Use bolding.
3. Samples will be held at a central laboratory so they can be re-tested for additional analyses should these become available. Destroyed after 5 years.
4. Please explain the process for following up and managing incidental findings.
5. Participants being recruited are routine outpatient appointments

Summary of ethical issues (outstanding)

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

1. The committee asked the researcher to explain the process for participants on placebo arm, and what occurs if they participate in the extension study.
2. The Committee queried how long participants have to consider participation.
3. The Committee noted that p.4.1 - the answer should include incidence and prevalence (statistics) of the disorder under study (or treatment indication if a drug trial) in Maori. The Secretariat notes that some disorders are particularly important for Maori health, while others are relatively rare in Maori and may have less of an impact. If the impact of treatment or prevalence of disease is low or the same as other populations please state this clearly to the Committee. Generally, any available statistics relating to Maori should be provided where possible.
4. Please note that health data derived from the study must be stored for a minimum of 10 years according to the [Health (Retention of Health Information) Regulations 1996](http://legislation.govt.nz/regulation/public/1996/0343/latest/DLM225650.html).

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

1. “However, possible benefits may get your condition better or worse during the study” – please revise document for language.
2. Explain that exams means physical examinations.
3. The Committee suggested including a diagram or table to show what happens at each visit. This can reduce repetition.
4. Please explain the process for following up and managing incidental findings.
5. Add contract details for the sub study. Do not refer to the main participant information sheet.

Decision

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

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

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

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| **4** | **Ethics ref:** | **15/NTA/213** |
|  | Title: | A Pilot study of a Probiotic for Eczema Treatment |
|  | Principal Investigator: | Dr Kristin Wickens |
|  | Sponsor: |  |
|  | Clock Start Date: | 14 January 2016 |

Dr Kristen Wickens and Mr Julian Crane 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. Phase I pilot study with 40 participants in New Zealand, 20 being children.
2. If left untreated in children, some eczema may lead to hospitalisation issues with children, hence the need for the trial
3. The medication is stated to be safe. The bacterial cell lysate is obtained by breaking open bacterial cells that contain anti-inflammatory substances. The lysate does not contain harmful substances.
4. Internal data safety monitoring.

Summary of ethical issues (resolved)

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

1. The Committee queried how potential participants are approached. The Researcher(s) explained the recruitment method, noting that researchers did not contact potential participants prior to them indicating they were interested in participating. The Committee was satisfied with the response.
2. The Committee queried if it was appropriate to encourage recruitment of Maori given that the study was about safety (phase I). The Researcher(s) explained the importance of having representative sample of New Zealand, for results to be generalizable, citing prevalence in Maori. The researchers explained that this is a low risk product. If we did not have a good sample size for Maori in the pilot then Maori may be disadvantaged as it could be unsafe to include Maori in the larger study. The Committee explained that Maori should not bare a disproportionate burden of research, but accepted the researcher’s explanation.
3. The Committee discussed sending the samples to Melbourne and whether they were for future unspecified research.
4. The Committee asked why data is stored in an identifiable form. The Researcher(s) stated it is stored in secure environment. If sending out to anyone else they would de-identify it.
5. (R.2.3) the Researcher(s) explained the means taken to ensure confidentiality.
6. The Committee discussed storage of tissue for this study. The Committee noted tissue could be stored for a period of time, while the researcher established a biobank application for submission in 2016. Because the tissue would be stored for this particular project the tissue could be stored without being an HDEC registered biobank. The Secretariat stated they would help the researchers set up their biobank.

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 samples cannot be stored for future unspecified research without a HDEC approved biobank. The Committee noted that the samples could be stored for this specific project in the existing facilities, and once a biobank had been established the participants could then consent for future storage and if necessary future unspecified research.
2. The Committee discussed the range of consent and assent forms, explaining:

Young people under the age of 16 may have the capacity to give valid consent, depending on their maturity and capacity to understand the nature and consequences of involvement in the study. However, committees recommend that researchers *also* get consent from the parents or guardians of children under the age of 16.

For adolescents between the ages of 14 and 16, the assent form should closely follow the consent form used for consenting adult participants.

For minors between the ages of 11 and 14 HDEC recommends using a simple written assent form.

If younger than 11 the HDEC suggests using a brief information sheet and consent form, where possible including pictures. This information is primarily used to assist a verbal assent process to gauge the child’s affirmation of participation.

For consent:

* Participant Information Sheet and Consent Form (this is used for adults or consenting adolescents)
* Parent or Legal Guardian Information Sheet and Consent Form (for consenting on behalf of children).

For assent:

* 5 - 7 year old assent form. Pictorial, one page.
* 12 - 15 Adolescent Participant Information Sheet and assent form. Simple language, short.

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

1. Add information on future use of tissue / swabs (under ‘what happens if I change my mind’).
2. Address both parents rather than just the mother (page 4).
3. Remove mention of money shortage for the assenting children.
4. Remove yes/no options from the consent form, unless they are truly optional.

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*).
* Remove the future unspecified research PIS/CF. They can be resubmitted as an amendment once the investigators have the appropriate regulatory approval to store tissue beyond the duration of a study.

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

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| **5** | **Ethics ref:** | **15/NTA/214** |
|  | Title: | OCR002-HE209: STOP-HE Study |
|  | Principal Investigator: | Prof Edward Gane |
|  | Sponsor: | Ocera Therapeutics, Inc. |
|  | Clock Start Date: | 14 January 2016 |

Ms Amy Cole and Ms Angela Lockie 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. Heptatis encephalopathy significantly reduces survival and irreversibly impairs thought processes in patients with cirrhosis (through build-up of ammonia and other toxins)
2. The new drug is intended to be an ammonia scavenger.
3. Participants are hospitalised in the liver unit at ACH
4. 230 participants worldwide. 4 participants will be recruited in New Zealand.
5. The study is approved in 16 other countries.
6. The Researcher(s) confirmed there was an independent data safety monitoring committee.

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 researchers agreed that the intended participants, due to their condition, are unlikely to be in a position to give informed consent.
2. While it is noted that relatives / caregivers can be consulted beforehand, to ascertain whether the participant might not want to be in trial, the caregiver cannot assent on the participant’s behalf.
3. The Committee requested that the researchers submit a cover letter explaining how the study meets right 7(4) of the code of rights or the 'best interests' test. The Committee noted they could not approve the study unless they were convinced that the study met this test, for each individual.
4. The Committee will not be able to approve any proxy consent documents as there is no legally authorised person in New Zealand who can do this for patients (for research). I have included this information below.

Right 7.4 of the HDC Code of Rights states that “Where a consumer is not competent to make an informed choice and give informed consent, and no person entitled to consent on behalf of the consumer is available, the provider may provide services where –

a) It is in the best interests of the consumer; and

b) Reasonable steps have been taken to ascertain the views of the consumer; and

c) Either, -

§ i. If the consumer's views have been ascertained, and having regard to those views, the provider believes, on reasonable grounds, that the provision of the services is consistent with the informed choice the consumer would make if he or she were competent; or

§ ii. If the consumer's views have not been ascertained, the provider takes into account the views of other suitable persons who are interested in the welfare of the consumer and available to advise the provider.”

1. Right 9 ensures that these rights extend to those occasions when a consumer is participating in, or it is proposed that a consumer participate in, teaching or research.
2. It is possible to approve a study (under Right 7.4) if it can be shown that participation is in the best interest of the consumer and they take into account the views of other suitable persons or believe that the consumer would wish to consent if they were able to. In these cases the consent can be provided by the clinician for this individual to participate in the research.
3. **With regards to proxy consent**, no one can consent on another adults behalf for research participation, including EPOAs or welfare guardians, let alone family members.
4. In general consent to a health care procedure need not be in writing but the exceptions include whether the procedure is experimental or for research (Right 7(6)).
5. Clause 4 of the Code provides that a person entitled to give consent on behalf of a consumer (which means a Welfare Guardian or EPOA) may act under Rights 5, 6, 7(1), 7(7) to 7(10) and 10. Accordingly the representative does not have the power to consent under Right 7(6).
6. Furthermore the Protection of Personal Property and Rights Act provides with regard to Welfare Guardians and EPOAs:

**“18 Powers and duties of welfare guardian"**

(1) No court shall empower a welfare guardian, and no welfare guardian shall have power,—

(f) to consent to that person’s taking part in any medical experiment other than one to be conducted for the purpose of saving that person’s life or of preventing serious damage to that person’s health.”

Decision

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

* Submit a cover letter outlining how participation is in the individual’s best interest, taking into account the law and legislation in New Zealand.

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

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| **6** | **Ethics ref:** | **15/NTA/215** |
|  | Title: | A study of GS-9620 in combination with Tenofovir Disoproxil Fumarate (TDF) for the Treatment of Participants with Chronic Hepatitis B and who are currently not on Treatment |
|  | Principal Investigator: | Prof Edward Gane |
|  | Sponsor: | Gilead Sciences, Australia & New Zealand |
|  | Clock Start Date: | 14 January 2016 |

Dr Hamilton and Ms Rebecca Hu were not 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 trial

1. A new medicine GS-0620
2. 17 participants in NZ. Ethics approval already given in the USA and Canada and is being sought in a further 6 countries
3. Four arms, the first arm being the standard TDK, with the other three arms being escalating dosages
4. The committee noted the comprehensive PIS describing in detail the previous trials and adverse events
5. The committee noted that Maori, Asian and Pacific Island people have a 10 fold higher of incidence as compared to Europeans.

Summary of ethical issues (outstanding)

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

1. Add lay language title.
2. The paragraph purpose of study. Make it clear that the drug is in combination with approved or already registered drug(s). The Committee noted this would likely be explained in the verbal processes for the HDEC.
3. The Committee noted that participants can withdraw from the study verbally, rather than in writing. While a written withdraw can be an option, participants always have the choice of verbally withdrawing, and this should be made clear to participants.

Decision

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

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| **7** | **Ethics ref:** | **15/NTA/216** |
|  | Title: | M15-410: A study of ABT-493/ABT-530 in chronic Hepatitis C patients who failed Direct-Acting Antiviral (DAA) therapy. |
|  | Principal Investigator: | Prof Edward Gane |
|  | Sponsor: | AbbVie Pty Ltd |
|  | Clock Start Date: | 14 January 2016 |

Dr Hamilton and Ms Carolyn Harris were not 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. Safety and effectiveness of two research drugs to treat HCV
2. Part 1 is already completed, This is Part 2 involving 80 participants worldwide with genotypes 1,4,5 & 6
3. Part 2, will involve 12 to 16 weeks of treatment
4. Already approved in USA and approval being sought in a further 6 countries including NZ
5. 5 participants will be recruited in NZ
6. The Committee noted that the information on Maori was of a very high standard, and commended the researchers.

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

1. The Committee requested the pregnancy information on the PIS/CFs are reviewed to ensure that it is relevant to the stage of the study that New Zealand participants will be involved in.

Decision

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

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| **8** | **Ethics ref:** | **15/NTA/217** |
|  | Title: | A study assessing the similarity of Avastin® and the trial drug BAT1706. |
|  | Principal Investigator: | Dr Chris Wynne |
|  | Sponsor: | Quintiles |
|  | Clock Start Date: | 14 January 2016 |

Dr Chris Wynne was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This is first in human study.
2. 129 healthy male participants between 18-50 years old.
3. The Researcher(s) explained the rationale behind comparing the study drug with different versions of Avastin. To have drug registered in Europe needs to be compared against European version, for FDA needs to be compared to American version. There should not be any difference between them but can’t get the new drug registered without comparisons.
4. The Committee noted while higher doses have side effects this is a low dose, with close monitoring of blood, urine and ECGs.

Summary of ethical issues (resolved)

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

1. R.1.5 The Committee noted the safety monitoring, including Representatives from sponsor, CRO and research team.
2. The Committee queried whether this BAT drug should have a better safety profile. The Researcher(s) stated no, it should be exactly the same.
3. The Researcher(s) explained the dosing plan, which enables safe and scientifically sound dosing.
4. The Committee commended the Participant Information Sheet.
5. The Committee asked if the drug manufactured is GMP certified. The Researcher(s) stated yes.
6. The Committee asked the researcher to remind the company of their ACC equivalent obligations, adding that the Committee expects any settlements to be made between company and participant rather than the participant and an insurer.

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

1. Amend the approving Committee to NTA.

Decision

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