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| **Committee:** | Central Health and Disability Ethics Committee |
| **Meeting date:** | 26 March 2019 |
| **Meeting venue:** | Room GC.3, Ground Floor, Ministry of Health, 133 Molesworth Street, Wellington |

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| **Time** | **Item of business** |
| 12:00pm | Welcome |
|  | Confirmation of minutes of meeting of 26 February 2019 |
| 12:30 | New applications (see over for details) |
| 12:30-12:55  12:55-1:20  1:20-1:45  1:45-2:10  2:10-2:35  2:35-3:00  3:00-3:25  3:25-3:50  3:50-4:15  4:15-4:40  4:40-5:05 | i 19/CEN/25  ii 19/CEN/27  iii 19/CEN/42  iv 19/CEN/33  v 19/CEN/34  vi 19/CEN/35  vii 19/CEN/37  viii 19/CEN/39  ix 19/CEN/47  x 19/CEN/49  xi 19/CEN/50 |
|  | Substantial amendments (see over for details) |
| 5:05-5:30pm | i 18/CEN/23/AM01 |
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|  | General business:  Noting section of agenda |
| 5:45pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Mrs Helen Walker | Lay (consumer/community perspectives) | 01/07/2015 | 01/07/2018 | Present |
| Mrs Sandy Gill | Lay (consumer/community perspectives) | 30/07/2015 | 30/07/2018 | Present |
| Dr Patries Herst | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | Present |
| Dr Dean Quinn | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | Present |
| Dr Cordelia Thomas | Lay (the law) | 20/05/2017 | 20/05/2020 | Present |
| Dr Peter Gallagher | Non-lay (health/disability service provision) | 30/07/2015 | 30/07/2018 | Present |
| Ms Helen Davidson | Lay (ethical/moral reasoning) | 06/12/2018 | 06/12/2021 | Present |

## Welcome

The Chair opened the meeting at 12:00pm and welcomed Committee members.

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 26 February 2019 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **19/CEN/25** |  |
|  | Title: | ANBL17P1 |  |
|  | Principal Investigator: | Dr Andrew Wood |  |
|  | Sponsor: | Children's Oncology Group (COG) |  |
|  | Clock Start Date: | 13 March 2019 |  |

Dr Andrew Wood and Sarah Hunter were present via 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

In this open-label non-randomised study, the researchers are seeking to determine whether dinutuximab and sargramostim can be added to the Children’s Oncology Group recommended induction chemotherapy for participants with high-risk neuroblastoma (NBL), without causing unacceptable side effects. How the cancer responds to the study therapy will also be examined.

Summary of resolved ethical issues

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

1. The Committee thanked the researchers for supplying a cover letter, and for its clarity.
2. The Committee commended the researchers on the table set out on page 4 of the PIS.
3. The Committee raised concerns over the use of previous consent for enrolment in future studies, and asked for assurance that there was some methodology to remind the participant that a generic consent form was already signed and that this consent can always be withdrawn, for both future unspecified and genetic research. The researchers confirmed that this would be done, and discussed with each individual study. Further, it was stated that each study participant, who is often involved in numerous studies, has a study folder which contains all signed consent forms. The Committee was satisfied with this, so long as participants are reminded of the ability to withdraw this consent at any time.
4. The Committee queried whether the CTSU form was covered by standard operating procedures or other relevant documentation. The researchers responded that it was covered in their own SOP.
5. The Committee queried whether participants are aware that their disease may return, as stated in the PIS. The researchers answered that participants are very aware of this, and that while distressing, they appreciate honesty in regards to this. The Committee noted that participants are currently being asked for consent to give additional samples if the disease returns in the future, and asked whether the research team would be able to discuss this consent with them again in this event. The researchers responded that in practice this discussion would not always take place, as it would depend on the individual coming back to their service. This is unlikely if they are over 20 and no longer coming to paediatric services. When the person is re-approached at 16 it is asked if they are still happy to have their samples stored; it is always acknowledged that consent is a process. The Committee asked how the researchers would know if the disease does return. The researchers answered that if the person is now out of the age range of their services they might never find out, though if they are registered in the New Zealand Children’s Cancer Registry this is benchmarked against the adult pathology registry, so if the person relapses and has tissue analysed the research team would be aware.

Summary of outstanding ethical issues

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

1. Please add to the 11-15 year old PIS the cultural paragraph (from the main PIS).
2. Please expand on the 11-15 year old PIS to reflect the higher level of understanding of this group (than the 7-10 year old group).
3. In the main PISCF, please arrange the order of content so that the main study consent section comes first, followed by consent for optional future unspecified research, followed by consent for bio-banking.
4. Please amend the final lines of page 11 of the parental PIS to simply state that “It is possible that the manufacturer may not continue to provide…”
5. Please remove the “if appropriate for this study” comment from the 7-10 PIS, as it relates to the side effect of the ability to have children.
6. The Committee *suggests* avoiding the repeated use of “high-risk neuroblastoma” by replacing it with the HRN acronym after its first use.
7. The Committee *suggests* placing contact details at the end of the 16 year old re-consent form.
8. Please change “to make sure everything is right for the study” to “to make sure everything is appropriate for the study” in regards to sending tumour samples overseas in the 11-15 year old PIS. On the following page, please also ensure that the sentence reads “if *you* and your parents or guardians agree”.
9. The Committee *suggests* removing the statement: “It is common to enrol children and adolescents in a clinical trial which seeks to improve cancer treatment over time.”
10. Please ensure that all PISs state where specimens are being sent, including where the centre is.
11. Please include in the main PIS information on participants’ rights to access information about themselves and to request corrections to this information. The HDEC template can be referred to if needed.

Decision

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

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

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| **2** | **Ethics ref:** | **19/CEN/27** |  |
|  | Title: | SNRIs for the treatment of osteoarthritis pain (STOP trial) |  |
|  | Principal Investigator: | Dr David Rice |  |
|  | Sponsor: | Waitemata District Health Board |  |
|  | Clock Start Date: | 28 February 2019 |  |

Dr David Rice and Dr Michael Kluger were present via 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

This is a two-arm randomised phase III study which aims to compare the effectiveness of Duloxetine to Venlafaxine for the treatment of knee osteoarthritis pain. In addition, it will test the function of specific pain pathways before treatment, to see if it can be predicted which individuals will benefit most from this treatment.

Summary of resolved ethical issues

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

1. The Committee observed that the application form indicated deception as an ethical issue in this study, but asked for clarity that this solely involved the use of a placebo in the study’s first week, followed by the drug in the weeks following, in order to ascertain participants’ pain pathways and establish an inpatient control. The researchers confirmed this, explaining that they are attempting to replicate a prior proof of principle study, which used the same method in a smaller population, as closely as possible. The benefit of this approach is that it gives a placebo response which can be controlled, and allows the research team to better delineate emerging adverse events. The Committee noted that this week of placebo, in conjunction with coming off pain relief in the week prior to the study, would mean that participants would be off pain relief medication for two weeks. It was asked for confirmation that, as per the protocol, participants would be able to take 3 consecutive days’ worth of paracetamol or other pain relief medication per week. The researchers confirmed this. The Committee noted that if the study drug was effective for, say, 40% of the participant population, then 60% would be without effective pain medication for the duration of the study. The researchers responded that in previous randomised controlled trials of Duloxetine both the placebo and active drug groups had access to rescue medication for up to 3 days in a row as proposed here – this is believed to be an acceptable rescue option for non-responsive participants which will also not jeopardise the scientific validity of the study.
2. The Committee commented that this study will use the HADS and Euroqol-5D questionnaires which contain questions about anxiety and depression. It was asked if these were necessary questions, and what safety plan was in place if participants were found to have severe anxiety and/or depression. The researchers conceded that this is an issue in many clinical studies, and that participants will have a contact number for the research nurse. If there is suspicion of extreme psychological distress either from the questionnaires or nurse review, then the researchers will contact the individual and also the primary care physician. The researchers added that an exclusion criterion for this study is a history of major psychiatric illness, and that therefore it is not anticipated that many people with severe anxiety or depression will be included.
3. The Committee noted that the answer supplied in question f.1.2 addresses the prevalence of osteoarthritis in Māori. However, the question is specifically concerned with other ethnicities, and the Committee asked the researchers to note this for future applications.
4. The Committee queried whether problems with the study drug related only to pregnancy, not to the fathering of children in general. The researchers said this was correct.

Summary of outstanding ethical issues

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

1. The Committee stated that the exclusion criteria should include contraindications to taking ibuprofen and paracetamol (*Ethical Guidelines for Intervention Studies* paragraph 5.41).

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

1. Please specify the amount of the gift voucher participants will receive.
2. The Committee *suggested* changing the title of the study from STOP to something more neutral.
3. Please include a statement of the participants’ right to access their personal information and request correction, in line with the Health Information Privacy Code.
4. Please add that the study will seek permission to communicate participation and results to GPs, as this is currently in the consent form but omitted from the PIS. Please note that nothing should appear in the CF which is not also discussed in the PIS.

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* paragraph 6.22).
* Please amend the exclusion criteria to include contraindications to taking ibuprofen and paracetamol (*Ethical Guidelines for Intervention Studies* paragraph 5.41).

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| **3** | **Ethics ref:** | **19/CEN/42** |  |
|  | Title: | National youth health and wellbeing survey |  |
|  | Principal Investigator: | Dr Deborah K McLeod |  |
|  | Sponsor: | Ministry of Social Development |  |
|  | Clock Start Date: | 07 March 2019 |  |

Dr Debbie McLeod and Tania Slater 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

This is a national survey of youth health and wellbeing, and will collect data from 14,000 12-18 year olds. Youth will be sampled through secondary schools, kura kaupapa youth service providers, and alternative education providers. The purpose of the study is to provide data on a range of priority areas that inform youth health and wellbeing policy work across government agencies. As parts of the survey will focus on health information, this study requires HDEC review.

Summary of resolved ethical issues

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

1. The Committee queried how it will not be known whether students have completed the survey if these are to be completed in a classroom setting, in the presence of others. The researchers responded that students have the option of declining to answer, but can still use the tablet device for other purposes. It will therefore not be known whether they have completed the survey or not.
2. The Committee confirmed that it was happy with the researchers using focus groups young people to inform the content of the survey, in order that a finalised version can be submitted to HDEC with the next application.
3. The Committee noted that the option is open to the researchers to remove health questions from the survey. The study would then cease to be heath research and would no longer be in tension with the *Code of Health and Disability Services Consumers’ Rights*.
4. The Committee was made aware that a study of this kind may have been previously approved by a different HDEC, and asked the researchers to provide evidence of this.

Summary of outstanding ethical issues

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

1. As the survey will be anonymised, and participants will be answering potentially distressing questions, the Committee expressed concern that no explicit safety plan was in place for participants who have a negative psychological reaction to the survey. The Committee noted the provision of relevant contact information and on-site mental health professionals, but would also like to see a safety mechanism whereby participants can identify themselves to a health professional for aid – whilst still preserving their study anonymity. For example, by providing a relevant form at the end, but independent from, the survey. (*Ethical Guidelines for Observational Studies* paragraph 5.5).
2. The Committee noted that many participants will be below the age of 16, and some will have cognitive disabilities. The participants must either be individually competent to consent to be a participant or their guardian must consent on their behalf. The researchers want to have an opt-out process for guardians The Committee noted that an opt-in by guardians consent model would severely impact the scientific validity of the study, and stated that it was willing to consider an opt-out approach if the other ethical issues raised in this discussion are met, and the means by which parents and guardians will be contacted, for example through advertising and social media, are submitted for review. In a new submission, the Committee also requests a clear argument as to why opt-out consent should be applied – this could include data of the effect on the participant population should opt-in consent be adopted. (*Ethical Guidelines for Observational Studies* paragraphs 1.9 and 6.10, and *Standard Operating Procedures for Health and Disability Ethics Committees* paragraph 42.4).
3. The Committee requested that the survey in its final form be uploaded for review, as it is not otherwise able to give approval (*Standard Operating Procedures for Health and Disability Ethics Committees* paragraph 42.4.6).

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

1. Please amend and expand the existing PISs using the HDEC template as a reference. Information to be added includes, but is not exclusive to, the HDEC, HDC, and Māori support contact numbers.
2. Please add headers and footers to the PISs, to better identify them.

Decision

This application was *declined* by consensus, as the Committee did not consider that the study would meet the following ethical standards:

* Please amend the information sheet and consent forms, taking into account the suggestions made by the committee (*Ethical Guidelines for Observational Studies* paragraph 6.10).
* Please add a safety mechanism whereby participants can identify themselves to a health professional for aid if required. For example, by providing a relevant form at the end, but independent from, the survey. (*Ethical Guidelines for Observational Studies* paragraph 5.5).
* Please demonstrate how it will be determined that all participants, on an individual basis, are competent to answer the questions in this survey. Alternatively, please provide to the Committee the means by which guardians will be contacted, for example through advertising and social media. A clear argument as to why opt-out consent is appropriate in this study should be forwarded in conjunction with this – possibly supported by research on the effect opt-in consent would have on consent by guardians. (*Ethical Guidelines for Observational Studies* paragraphs 1.9 and 6.10, and *Standard Operating Procedures for Health and Disability Ethics Committees* paragraph 42.4).
* Please provide the survey in its final form for review (*Standard Operating Procedures for Health and Disability Ethics Committees* paragraph 42.4.6).

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| **4** | **Ethics ref:** | **19/CEN/33** |  |
|  | Title: | Randomised controlled trial of prescription charges |  |
|  | Principal Investigator: | Professor Pauline Norris |  |
|  | Sponsor: | University of Otago |  |
|  | Clock Start Date: | 14 March 2019 |  |

Professor Pauline Norris and Kim Cousins were present via 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

This is a randomised controlled trial of prescription charges to determine whether removing charges would improve people’s health. Recruitment will target a group of people who have diabetes and/or ongoing mental health conditions requiring medication, and who live in deprived neighbourhoods. Half will act as a control group, and the other half will have their prescription charges paid for a year. Additional differences in health services use, quality of life, and medicines use between the groups will also be investigated.

Summary of resolved ethical issues

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

1. The Committee queried whether problems were foreseen with people not wanting to be in the control group. The researchers responded that they aware of this possibility, but that the feasibility study did not indicate any problems and the future $100 payment was a strong incentive for participation.

Summary of outstanding ethical issues

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

1. The Committee advised that qualifiers such as ‘low income’ or high-deprivation’ be removed from study advertisements to avoid stigmatisation. Alternatives such as ‘suitable’ or ‘selective’ participants could be used. (*Ethical Guidelines for Intervention Studies* paragraph 6.2).

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

1. Please amend to state that participants will not be able to choose which group they will be assigned to in the study.
2. Please include information on and secure consent for the interviews to be conducted for the purposes of this application.
3. Please add extra information, including details of how and where information will be stored, who has access to it, confidentiality, and so on. For guidance on this extra information, please refer to the HDEC PISCF template. An ACC statement should also be added.
4. Please amend the statement about participants who start medication because of this study to “If you are able to start taking medication where you were previously not, you may need to discuss this with your doctor”, or something similar.
5. Please add to the consent form that permission will be sought to communicate any serious psychological reactions to the study interviews to the participant’s GP.

Decision

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

* Please avoid qualifiers such as ‘low income’ or high-deprivation’ in study advertisements to avoid stigmatisation. Alternatives such as ‘suitable’ or ‘selective’ participants could be used. (*Ethical Guidelines for Intervention Studies* paragraph 6.2).
* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* paragraph 6.22).

After receipt of the information requested by the Committee, a final decision on the application will be made by Ms Helen Davidson and Dr Dean Quinn.

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| **5** | **Ethics ref:** | **19/CEN/34** |  |
|  | Title: | VStim MCI |  |
|  | Principal Investigator: | Dr Denise Taylor |  |
|  | Sponsor: | Auckland University of Technology |  |
|  | Clock Start Date: | 14 March 2019 |  |

Dr Denise Taylor was present via 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

This study will use a sub sensory threshold stimulation delivered to the vestibular system that aims to boost weak sensory signals from the vestibular system, such that they can be utilised in spatial memory. It is hoped that this will improve gait and balance in people with mild cognitive impairment.

Summary of outstanding ethical issues

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

1. The Committee observed that participants will be recruited through the Dementia Prevention Research Centre Database, and that the researchers must be satisfied that the participants are able to give informed consent. The Committee noted that patients on this database are reviewed every 6 months by the centre, but believed that this may not be sufficient as an assessment of competence, with a potential delay of up to 6 months between review and commencement of the study. The Committee requested that individuals be screened for competence by the research nurse prior to entering the study, and that all exclusion criteria are checked for in the pre-screening process. (*Ethical Guidelines for Intervention Studies* paragraphs 5.41 and 6.22).

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

1. Please add a footer with version and date.
2. Please add contact details for Māori support.
3. Please remove tick boxes for aspects of the study which are not truly optional.
4. Please use a lay-person title of and explanation for the study device. ‘Spatial navigation’ should also be explained for a lay-readership, and terminology and language should be simplified in general.
5. The Committee *suggests* including a diagram of the study design, to improve understanding.
6. Please include in the PIS information on participants’ rights to access information about themselves and to request corrections to this information in accordance with the Health Information Privacy Code.

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* paragraph 6.22).
* Please ensure that individuals are screened for competence by the research nurse prior to entering the study, and that all exclusion criteria are checked for in the pre-screening process. (*Ethical Guidelines for Intervention Studies* paragraphs 5.41 and 6.22).

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| **6** | **Ethics ref:** | **19/CEN/35** |  |
|  | Title: | TAF breast milk PK |  |
|  | Principal Investigator: | Prof Ed Gane |  |
|  | Sponsor: | Auckland District Health Board |  |
|  | Clock Start Date: | 14 March 2019 |  |

Professor Edward Gane, Sarah Coates, and Julianne Brewer were present via 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

This is a pilot study to investigate whether tenofovir disoproxil fumurate, a recommended antiviral prophylaxis, can be detected in breast milk or in the urine of breast-fed babies. The study will also test the mother’s blood for presence of the drug.

Summary of resolved ethical issues

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

1. The Committee noted that the cultural questions section in the application was not answered particularly well. Questions p.4.1 and f.1.2 should have provided statistics on the prevalence of HCB in Māori and other ethnic populations respectively, and question p.4.2 should have identified that the taking and sending of tissue overseas was a cultural issue for Māori.

Summary of outstanding ethical issues

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

1. Please add a consent box to the PIS to be completed following the birth of the child, allowing information on that child to be collected.
2. Please add that samples will be sent overseas.
3. Please amend the infant PISCF, which appears to have sections which have been cut and pasted from the mother’s PISCF. Please use consent/assent where appropriate.

Decision

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

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

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| **7** | **Ethics ref:** | **19/CEN/37** |  |
|  | Title: | ONS-5010: Efficacy and safety of ONS-5010 in subjects with subfoveal choroidal neovascularization (CNV) secondary to age-related macular degeneration. |  |
|  | Principal Investigator: | Prof Philip Polkinghorne |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 14 March 2019 |  |

Professor Philip Polkinghorne was present via 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

This study will assess the efficacy and safety of intravitreal injections of ONS-5010 (an ophthalmic specific bevacizumab), compared with ranibizumab in subjects with primary or recurrent subfoveal choroidal neovascularization. Only one eye will be chosen as the “study eye” and will receive an injection of ONS-5010 or ranibizumab.

Summary of resolved ethical issues

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

1. The Committee queried whether participants, who suffer from macular degeneration, will be able to adequately read the patient information sheet and consent form. The researchers answered that it will either be read it large font, or the contents will be read to them.
2. The Committee commented that in question p.4.1 of the application form, which asks what benefit this study may have for Māori, that it would have preferred to have seen statistics about the prevalence of age-related macular degeneration in Māori.

Summary of outstanding ethical issues

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

1. The Committee asked for clarification of whether the study drug has or is being reviewed by SCOTT for this use (*Ethical Guidelines for Intervention Studies* Appendix 1).

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

1. Please reduce the length and complexity of the study title.
2. Please amend the opening paragraphs so that they are appropriate for a lay-readership.
3. Please state clearly that ACC eligibility does not apply in this clinical trial. The HDEC template offers guidance on wording.
4. Please add on page 4 that an early withdrawal visit will be conducted *with consent*.
5. Please add both information on tissue being sent overseas and a cultural statement for Māori regarding this on the consent form.
6. Please clarify that the study will fund taxi journeys to the clinic and home again.
7. Please supply an information sheet and consent form for the pregnant partner, and either an additional PIS or additional consent box in the existing PIS to be signed by the parent or guardian for use of the child’s information after that child has been born.
8. Please make clear that payment is being made to the Auckland eye facility for nursing expenses etc.
9. Please make clear in the consent form that additional information may be requested from participants’ GPs.

Decision

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

* Please clarify whether the study drug has or is being reviewed by SCOTT for this use (*Ethical Guidelines for Intervention Studies* Appendix 1).
* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* paragraph 6.22).

After receipt of the information requested by the Committee, a final decision on the application will be made by Ms Helen Davidson and Dr Dean Quinn.

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| **8** | **Ethics ref:** | **19/CEN/39** |  |
|  | Title: | TORPIDO 30/60 |  |
|  | Principal Investigator: | Dr Bronwyn Dixon |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 14 March 2019 |  |

Dr Jane Alsweiler, Professor William Tamow-Mordi, and Melinda Cruise were present via 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

This study aims to compare short and long-term outcomes of 1470 preterm infants born less than 29 weeks gestation who have had respiratory care in the delivery room. The primary composite outcome of interest is death or survival free from major brain injury, with the secondary outcomes being all-cause mortality and major brain injury. Consent is not intended to be sought from guardians prior to infants being placed on oxygen.

Summary of resolved ethical issues

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

1. The Committee queried why an observational study of existing data of survival rates could not be done to supply the current proposal with preliminary evidence regarding oxygen levels. The researchers replied that an observational approach is not sufficiently reliable, and contains too many variables to draw reliable inferences. Some meta-analyses suggest that 60% may be preferable to 30%, but a randomised trial is the only way to establish the best method.
2. The Committee advised that in future application forms, for question p.4.1 it is not appropriate to reference the Treaty of Waitangi, this is rather a question about how the study might improve health outcomes for Māori. Additionally, question p.4.2 should address how study processes will impact Tikanga Māori, such as aspects which may be considered tapu, induce whakamā, and so on. The Treaty need not be referenced here either.

Summary of outstanding ethical issues

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

1. The Committee accepted that this is a very worthwhile study, and that there is great importance in determining the safest and most effective level of oxygen to be delivered to preterm infants. The Committee appreciated that the researchers wish to perform this study to the highest level of scientific validity, that if consent is sought from parents this will introduce post-randomisation exclusion bias and a likely failure to meet recruitment targets, and that the negligible window of time open to secure consent prior to oxygen treatment makes this practically impossible. It was noted that previous studies adopting a “traditional” approach of prior parental consent had these difficulties confirmed. The problem that there exists no standard practice was also acknowledged by the Committee. However, the Committee informed the researchers that, in order to proceed with this study without the prior consent of a parent or guardian, an argument must be made pursuant to Right 7(4) of the Code of *Health and Disability Services Consumers’ Rights*. Therein, the researchers must establish that it is in each individual infants’ best interest to participate in this study, i.e. that they would be better off being included in this study than not. The Committee registered the researchers’ argument that this research has the capacity to save future lives and is of great public benefit, but clarified that the Code requires that the research be in the *individual’s* best interest. The researchers’argument that participation in a phase III study has been empirically proven to be of benefit to the individual did not satisfy the Committee. The Committee explained that it welcomes a resubmitted application with accompanied New Zealand legal advice around Right 7(4). (*Ethical Guidelines for Intervention Studies* paragraph 1.10).
2. The Committee noted that there is an additional problem with the intention to use infants’ health information with an opt-out consent model (*Ethical Guidelines for Intervention Studies* paragraph 6.22).
3. The Committee advised that in a resubmitted application, the researchers will also need to justify the use of deception. Specifically, in regards to not later disclosing to parents which group their child was allocated to. (*Ethical Guidelines for Intervention Studies* paragraph 6.31).

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

1. Please re-examine the PIS following the guidance of the HDEC template.

Decision

This application was *declined* by consensus, as the Committee did not consider that the study would meet the following ethical standards:

* In the resubmitted application, please forward an argument which establishes, under the HDC Code, that consent for the infants’ participation can be waived with reliance on Right 7(4). Reputable legal advice should be sought to lend support to this argument. (*Ethical Guidelines for Intervention Studies* paragraph 1.10).
* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* paragraph 6.22).
* Please provide an argument which establishes the appropriateness of opt-out consent in this context (*Ethical Guidelines for Intervention Studies* paragraph 6.22).
* Please justify the use of deception, in relation to not informing parents of which group their child was randomised to (*Ethical Guidelines for Intervention Studies* paragraph 6.31).

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| **9** | **Ethics ref:** | **19/CEN/47** |  |
|  | Title: | The Koru Study |  |
|  | Principal Investigator: | Mrs Ciara Funnell |  |
|  | Sponsor: | Massey University |  |
|  | Clock Start Date: | 14 March 2019 |  |

Dr Louise Brough and Ciara Funnell were present were present for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

This study will measure dietary intake during each trimester of pregnancy to investigate the drivers of gestational weight gain. It will also investigate the maternal intake and status of micronutrients which are of concern for pregnant women in New Zealand (iron, iodine, selenium, and folate). The study will determine energy expenditure by measuring physical activity during each pregnancy trimester in conjunction with energy intake. Additionally, it will investigate whether the gestational weight gain guidelines and dietary advice has been discussed with pregnant women by a health care professional.

Summary of resolved ethical issues

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

1. The Committee noted that the scientific peer review of this study recommended narrowing the time range for participants to present for visit 4. The researchers responded that they have heeded this advice, and changed the window from 7-21 days to 7-14 days. The Committee also noted that the peer review recommended the accelerometer to be worn for all participants at each time point. The researchers stated that this was always the intention.
2. The Committee advised that it would have been useful to see information on body composition etc. in Māori and other ethnicities in the cultural questions section of the application.
3. The Committee queried whether the researchers think the participant population will “self-select” from leaner pregnant mothers, as overweight mothers might avoid this study due to stigmatisation. The researchers responded that this is a possibility, but even if there is a bias in the population the study will still generate interesting information. When publishing, the researchers advised that they would be mindful of this potential bias. The Committee noted that the advertisements avoid embarrassing terminology which may help to mitigate this bias.
4. The Committee advised the researchers that, alongside cultural issues relating to the collection and use of tissue, both whakamā (embarrassment or shame) and the participating women being whare tapu (the womb of life) will be salient issues for Māori.

Summary of outstanding ethical issues

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

1. Please review the document for spelling and grammatical errors.
2. Please explain why “it is essential that we understand both weight and body composition changes through pregnancy.”
3. Please reword the statement that observational research does not involve anything beyond what participants would otherwise do.
4. Please include information on who will collecting blood samples – i.e. the trained phlebotomists.
5. Please explain that results of the haemoglobin testing will be given to participants immediately, and that any abnormal results from other tests will be communicated to participants at a later point.
6. Please amend to reflect that parents cannot consent on behalf of the child prior to its birth. Consent should be secured first for the collection of the mother’s data during pregnancy, and after the child is born secured for use of the child’s data. The separate PIS for the child should only include information relevant to the child.
7. Please amend the statement on page 3 to state that participants will be *asked* to place the accelerometer machine on their wrists.
8. Please fix the ambiguity in the statement about participants being in the human nutrition research unit “when the baby is born”, so that it is clear the birth will not happen here.
9. Please amend the statement in the rights sections of the PIS, to state that consent can be withdrawn at *any* time, not only when it is practicable.
10. Please remove any tick boxes in the consent form for aspects of the study which are not truly optional.
11. Please make clear that the population group of 102 refers to the mothers, not the potential children.
12. Please add as a tick box for the mother’s PIS consent to give access to the child’s information. This can lead into the PIS exclusively for the child’s health.
13. Please add a statement that in the event of a miscarriage or stillbirth the mother’s data may not be included in the study. Additionally, a preterm birth may have an effect on study results. The dependencies for continued participation in general should be made clear.
14. Please add that little research on body composition in pregnant women has been done.
15. Please make clear that the samples stored will be used only for future analyses related to this study, and that they will not be used for future unspecified research.
16. Please include the amount of the Koha.
17. Please add that informed consent will be sought to inform participants’ GPs of their participation in this research.
18. Please add a Māori cultural statement concerning the use of tissue. The HDEC PISCF template offers guidance on this.
19. Please be clear that this study is related to a PhD qualification.

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* paragraph 6.10).

After receipt of the information requested by the Committee, a final decision on the application will be made by Dr Cordelia Thomas and Dr Patries Herst.

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| **10** | **Ethics ref:** | **19/CEN/49** |  |
|  | Title: | TROG 17.06 - SC.24 SBRT vs CRT for patients with spinal mets |  |
|  | Principal Investigator: | Dr Louis Lao |  |
|  | Sponsor: | TranTasman Radiation Oncology Group |  |
|  | Clock Start Date: | 14 March 2019 |  |

Dr Louis Lao and Sophie Goodger was 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

This is a phase III study comparing standard practice Conventional Palliative Radiotherapy to Stereotactic Body Radiotherapy which is delivered in fewer treatment visits but at higher doses than current standard practice. Patients with cancer who have documented spinal metastases will be eligible for this trial. Along with pain response the study will also measure patient experience through questionnaires.

Summary of resolved ethical issues

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

1. The Committee asked the researchers to note that the phrase “Māori will be given equal rights to participate” is patronising and unnecessary, and should not be included in future applications for question p.4.1, which asks for statistics concerning prevalence of the study disease in the Māori population.

Summary of outstanding ethical issues

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

1. The Committee requested that the HDEC scientific review template be forwarded to the TROG lead reviewer for completion (*Ethical Guidelines for Intervention Studies* Appendix 1).

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

1. On the general information form: please remove the term “legally authorised person” from page 3, as this is not a legal concept in New Zealand for adult participants in research that is a “medical experiment”; please amend the definition of informed consent on page 4, in line with Right 6(1) of the HDC *Code of Health and Disability Services Consumers’ Rights* (“information that a reasonable consumer, in that consumer’s circumstances, would expect to receive”); please amend or remove references to the age of consent, to reflect New Zealand law (16 years of age); please amend the final bullet point on page 6, as HDECs do not review applications for scientific validity.
2. On the PIS: please check the paragraph on page 12 regarding ‘pain flare’ for syntax and grammar; please change the description of the side effect on page 13, cited as occurring in 1 of 100 individuals, from “very rare” to simply “rare”; please amend the sentence for female participants on page 13 – “if you become pregnant and do not want the researchers to collect this information…” – to reflect *opt-in* consent, for example “will ask permission to collect…” (the same logic should be followed for access to all information); please amend to reflect that consent for a child’s information can only be given by a parent or guardian following the birth of that child; please amend the ACC statement to state that participants will be eligible to *apply* of compensation; please remove references to future unspecified research from the main PIS, as this is covered in the separate document.

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* paragraph 6.22).
* Please ensure that the HDEC scientific review template is forwarded to the TROG lead reviewer for completion (*Ethical Guidelines for Intervention* *Studies* Appendix 1).

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| **11** | **Ethics ref:** | **19/CEN/50** |  |
|  | Title: | Cabozantinib plus Atezolizumab for advanced liver cancer |  |
|  | Principal Investigator: | Professor Edward Gane |  |
|  | Sponsor: | Pharmaceutical Research Associates Ltd |  |
|  | Clock Start Date: | 14 March 2019 |  |

Professor Edward Gane, Sarah Coates, and Sarah Middleton were present via 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

This study will compare the efficacy of cabozantinib, in combination with atezolizumab, with sorafenib in individuals with advanced hepatocellular carcinoma who have not received previous systemic anticancer therapy. Additionally, there will be an exploratory arm to evaluate the single-agent safety and activity of cabozantinib.

Summary of resolved ethical issues

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

1. The Committee observed that a quality of life questionnaire in this study contains questions around anxiety and depression, and queried what safety plan was in place if a participant indicated severe anxiety or depression. The researchers responded that they have good access to both liaison psychiatry and community mental health. The Committee questioned whether the survey is reviewed by computer, or whether someone will be in a position to identify a need for follow up manually. The researchers answered that a study nurse will be reviewing the questionnaires.

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

1. Please amend page 15, stating that participants’ doctors will be asked to collect data on their babies *with their consent*.
2. Please review the pregnant partner and infant PISCFs, ensuring that they contain only relevant information for the target person, and refer to them appropriately. Please note as well that either parent can give consent for the infant, not only the mother.

Decision

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

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

## Substantial amendments

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| **1** | **Ethics ref:** | **18/CEN/23/AM01** |  |
|  | Title: | Campylobacter and Frailty |  |
|  | Principal Investigator: | Dr Tim Frendin |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 06 February 2019 |  |

Dr Tim Frendin was present via 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.

One member declared a potential conflict of interest and the Committee decided to continue the discussion without their participation.

Summary of Amendment

As the study has been unable to meet recruitment targets, a request is being made to include the data of ‘control’ individuals without their consent.

Summary of outstanding ethical issues

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

1. The Committee appreciated that the process for securing consent in the control group has been difficult, but was not convinced by the researcher’s argument that this is an audit. As nothing in the data of the control group is being specifically audited, and these data are being accessed solely to act as a control, this is an observational study. Further, the Committee did not believe it was justified to include the health information of people who had already declined to have their data accessed for this study, or even for those not yet approached. The Committee believed that the nature of the study required consent, and that other avenues were open for seeking consent, such as presenting the study at rest homes or accessing patients via their GPs. (*Ethical Guidelines for Observational Studies* paragraphs 6.10 and 6.43).

Decision

This application was *declined* by consensus, as the Committee did not consider that the study would meet the following ethical standards:

* The Committee judged that it could not grant a waiver of consent while reasonable options were open to the researcher to seek informed consent from the control group (*Ethical Guidelines for Observational Studies* paragraphs 6.10 and 6.43).

## 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:** | 26 April 2019 |
| **Meeting venue:** | Room GC.3, Ground Floor, Ministry of Health, 133 Molesworth Street, Wellington |

The following members tendered apologies for this meeting.

* Dr Peter Gallagher

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 5.30pm.