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| **Committee:** | Central Health and Disability Ethics Committee |
| **Meeting date:** | 24 April 2018 |
| **Meeting venue:** | Room GN.6, Ground Floor, Ministry of Health, 133 Molesworth Street, Wellington |

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| **Time** | **Item of business** |
| 12.00pm | Welcome |
| 12.05pm | Confirmation of minutes of meeting of 27 March 2018. |
| 12.30pm | New applications (see over for details) |
|  | i 17/CEN/229  ii 18/CEN/54  iii 18/CEN/57  iv 18/CEN/60  v 18/CEN/62  vi 18/CEN/63  vii 18/CEN/64  viii 18/CEN/65  ix 18/CEN/67  x 18/CEN/68  xi 18/CEN/69  xii 18/CEN/71 |
| 5.30pm | Review of approved studies (see over for details) |
|  | xiii 18/CEN/72 |
| 5.45pm | General business:   * Noting section of agenda |
| 6.00pm | 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 |
| Dr Angela Ballantyne | Lay (ethical/moral reasoning) | 30/07/2015 | 30/07/2018 | 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 Melissa Cragg | Non-lay (observational studies) | 30/07/2015 | 30/07/2018 | Present |
| Dr Peter Gallagher | Non-lay (health/disability service provision) | 30/07/2015 | 30/07/2018 | 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 27 March 2018 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **18/CEN/54** |
|  | Title: | COG: Pαβlo |
|  | Principal Investigator: | Dr Lochie Teague |
|  | Sponsor: | ANZCHOG |
|  | Clock Start Date: | 12 April 2018 |

Dr Lochie Teague and Ms Paula Murray 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. The primary purpose of this trial is to evaluate the efficacy of using parent donors for bone marrow transplants in children, using a particular processing method of the donor blood cells (TCR α+ß+/CD19+ cell depletion) compared to those receiving a standard bone marrow transplant from another donor.
2. The Researcher(s) also want to compare costs to the health system of TCR α+ß+/CD19+ cell depletion with that of standard bone marrow transplant procedures. However, the cost comparison part of the study will be undertaken in Australia with the results shared to New Zealand.
3. Patients who have no fully matched sibling, and no well-matched volunteer donor or umbilical cord blood unit available will receive a TCR α+ß+/CD19+ cell depleted graft from a parent donor. Control patients will receive a standard bone marrow transplant from another donor (e.g., volunteer donor) as per institutional practice.
4. Patients will undergo clinical assessments at regular intervals for two years following the transplant to evaluate the efficacy of the treatment. Further information, such as quality of life and carer burden, will be collected for up to 5 years following the transplant.
5. It is hoped that the findings from this trial will provide information on whether parent donor cells undergoing specialised cell processing can be effectively used for bone marrow transplants in children with haematological malignancies or non-malignant disorders.
6. The Committee thanked the Researcher(s) for the cover letter.

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 for more information about the study arms. The Researcher(s) explained the rationale for the decision of each study arm, noting the cost comparison part of the study.
2. The Researcher(s) explained that the main focus is a proof of principle, in relation to satisfactory graphing.
3. The Committee asked about the role of Miltenyi Biotech. The Researcher(s) explained that the company provides the machinery that allows us to perform the procedure. There are a couple of suppliers in the world. Their involvement allowed us to conduct the study; they have provided use of the machine free of charge. The Researcher(s) added they would have had to use their machines in any case.

Summary of ethical issues (outstanding)

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

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

Main participant information sheet

1. Page 1 ‘*some patients don’t have any of these donors available, this may be the case for you*’. The Committee noted that this would not be the case for the controls. The Researcher(s) noted they would remove the last sentence for the control participant information sheet. Similarly, ‘*this may be the case for you*’ should be changed to will, for the intervention arm. The Researcher(s) noted this, adding it was a legacy from a master, and a cut and paste error.
2. Page 5 states that data is disposed of after 5 years. The Committee noted that usually the duration is 10 years after child turns 16. The Researcher(s) noted on page 4 – it is stated that data will be stored for 10 years from time youngest participant turns 16. The Committee acknowledged this, but noted it was confusing having both statements. Please remove the study centre one (5 years). The Researcher(s) agreed and confirmed they would amend the wording.
3. Please add the country samples were stored in (Sydney). This is applicable to all participant information sheets where relevant.
4. The Committee asked whether it was appropriate to list side effects of treatments that were part of standard of care. The Researcher(s) and The Committee discussed this and determined that they are still possible outcomes, while it is intrinsic to those conditions and treatments, it also is a result from the treatments received in the study.
5. Participant information sheet refers to ‘your disease’. The Committee asked if this was the most appropriate language. The Researcher(s) explained the rationale, and that it was normal in this clinical context. The Committee accepted this response.

Decision

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

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| **2** | **Ethics ref:** | **18/CEN/57** |
|  | Title: | COG AALL1631 |
|  | Principal Investigator: | Dr Peter Bradbeer |
|  | Sponsor: | Children's Oncology Group (COG) |
|  | Clock Start Date: | 12 April 2018 |

Dr Lochie Teague and Ms Sonia Alix 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. Approximately 3-5% of paediatric acute leukaemia and lymphoma (ALL) patients present with the Philadelphia chromosome (Ph+ ALL). Historically, patients with Ph+ ALL had a poor outlook and were considered candidates for stem cell transplant (SCT) after there were no signs of leukaemia in their blood (remission).
2. Studies conducted by COG and the European EsPhALL consortium over the last decade have shown that the majority of paediatric Ph+ ALL patients are effectively treated with the combination of a medicine called a tyrosine kinase inhibitor (TKI, in this study imatinib) and chemotherapy, without SCT.
3. However, the chemotherapy administered in these trials was more intensive than what is standardly used for non-Ph+ paediatric ALL. This intensive chemotherapy resulted in high rates of treatment-related toxicities (including life-threatening infections) and death, as well as increased risk of late side effects.
4. Reducing the treatment-related toxicity, without compromising disease free survival would be an important advancement for this patient population. AALL1631 will study the effects of a less intensive chemotherapy together with imatinib in standard risk (SR) patients, as well as the effects of the use of imatinib alone after SCT in HR patients.

Summary of ethical issues (outstanding)

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

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

1. The Committee queried whether it is coercive to state that “*It is common to enrol children and adolescents with cancer in a clinical trial that seeks to improve cancer treatment over time.’’* The Committee suggested ‘it is not unusual to enrol’. The Committee note this is a minor, optional, suggestion.
2. The Committee noted that the current participant information sheet wording was confusing with respect to the different optional sub-studies, in particular in relation to tissue. The Researcher(s) explained the different parts of the study, referring to three levels of use of tissue. The Committee requested that the documentation is reviewed, to make it very clear: what samples were taken, when, how they were used for the study and how they would be used for any involvement in the various sub-studies. In particular, page 48 is confusing and could be reworded. In this section it should cover the genetic tests, not the bio-banking, which is outlined clearly in the optional separate 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 forms, taking into account the suggestions made by the Committee (Ethical Guidelines for Intervention Studies para 6.22).
* Provide a cover letter to HDEC explaining the sub-studies and their use of tissue and explain the changes that have been made to aid clarity for participants when providing consent to participate.

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

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| **4** | **Ethics ref:** | **18/CEN/60** |
|  | Title: | Neurodevelopmental outcome study of neonates with hypoxic ischemic encephalopathy and seizures from the NEOLEV2 trial |
|  | Principal Investigator: | Dr Cynthia Sharpe |
|  | Sponsor: |  |
|  | Clock Start Date: | 12 April 2018 |

Dr Cynthia Sharpe 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 NEOLEV2 randomized control treatment trial studying the efficacy of Phenobarbital and levetiracetam in neonatal seizure cessation is now complete. The Researcher(s) propose a neurodevelopmental follow up study of patients in NEOLEV2 who had Hypoxic ischemic encephalopathy or seizures. With consent, the Researcher(s) would review the medical records of this cohort of babies and gather data on rates of post neonatal epilepsy, cerebral palsy and other neurodevelopmental disabilities.
2. Consenting families are to be interviewed to gather additional information about breast feeding and postpartum bonding experiences. The Researcher(s) would conduct neurodevelopmental testing on the Auckland subjects. These additional data, in addition to the rich dataset created during the NEOLEV2 study, would allow the Researcher(s) to look at multiple important research questions:
   * + Are neonatal seizures damaging? Do infants with seizures in addition to hypoxic ischemic encephalopathy have worse neurodevelopmental outcomes than infants with the same severity of hypoxic ischemic encephalopathy but no seizures?
     + Is intensive cEEG monitoring important? Do babies who have a longer lag between the onset of their seizures and their detection and treatment have worse outcomes than babies whose seizures are recognised immediately?
     + Can intensive cEEG monitoring be targeted to those most at risk, sparing resources? If the first hour of the EEG monitoring is normal, does that predict reliably that the baby will not have seizures and that monitoring can be less intensive or discontinued?
     + Do babies who were randomized to receive Levetiracetam have better neurodevelopmental outcomes than babies who were randomized to Phenobarbital?
     + Do breastfed infants in this high-risk cohort have better neurodevelopmental outcomes, and better maternal infant bonding outcomes?

Summary of ethical issues (resolved)

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

1. The Committee explained that potential benefit for Maori is not only with respect to those in study but wider Maori population. Therefore, incidence would have been helpful in answering the application questions, and understanding of cultural aspects, such as whakama – shame, due to injury, would have also reflected good practice.

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 for comments or feedback from the funding bodies that provided peer review.
2. The Committee noted that researchers did need to consult with Maori.
3. The Researcher(s) noted no current research on incidence for Maori.

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

1. The Committee noted that while the participant information sheet states that the reason for the study is to follow up from a previous study, the application form itself is much more expanded in outlining the study aims and rationale. The application notes, for example, reviewing medical records, gathering additional data, interviews etc.
2. The Researcher(s) explained the different aspects of the study, including the breastfeeding relationship with brain injury outcomes, and maternal bonding.
3. The Researcher(s) noted there would be limited study staff involved in bonding questionnaires / interviews to reduce harm.
4. The Researcher(s) explained the rationale for retrospective record review.
5. The Researcher(s) explained the study aims in relation to neuropsychological evaluations and the important neurodevelopment outcomes.
6. The Committee noted that the participant information sheet should outline exactly what is occurring and why. The Committee asked that all of the aspects of the study are added to the participant information sheet, noting it currently focuses on breastfeeding, not these other factors.
7. The Committee suggested actually adding the 5 research questions in the application in the participant information sheet. The Committee noted less emphasis on breastfeeding is also beneficial due to a reduction in potential stigma of those who did not breastfeed.
8. Pg.2 under risks and benefits - this study may ‘*uncover sadness’* and refers to ‘*skilled councillor’.* Please rephrase, as it is not clear who is a skilled councillor also it is not necessarily the case that it uncovers sadness. The Committee suggested *‘may bring up issues’*.
9. The Committee noted that the participant information sheet could be improved by using the HDEC template for informed consent, found at <https://ethics.health.govt.nz/guides-templates-forms-0>. For example, please add a list of contact details at the end of the participant information sheet for important support groups, for example Maori support.
10. Please revise the yes and no tick boxes on the consent form and remove the option if the statement is not truly optional.
11. Add in participant information sheet that parts of the study are optional, and explain which parts are optional more clearly.
12. The Committee requested the compensation wording is updated for accuracy, they suggested the following statement: *“If you were injured in this study, which is unlikely, you would be eligible* ***to apply*** *for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery. If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.”*
13. Page 2 of 5 states agree to follow up if still willing. The Committee asked whether participants from the original study consented to be contacted or consented to be part of future studies. The Researcher(s) stated consented to be contacted. Please reword, implies that they consented for research not just to be contacted.
14. Please add sentence that participants ‘can refuse to answer any questions’ following the explanation that some may be hard or challenging to answer.
15. The Committee asked whether interviews are conducted at participant’s home or in clinic. The Researcher(s) stated that while they follow many of these children clinically, most interviews will be completed by phone or by home visit.
16. The Committee noted in the event that a participant does come into clinic for research purposes they should be reimbursed.
17. The Committee noted that the need to store health information for 10 years following turning 16 is not a legal requirement.

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).

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

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| **4** | **Ethics ref:** | **18/CEN/62** |
|  | Title: | Trio WES in ultra-rare genetic syndromes |
|  | Principal Investigator: | Dr Patrick Yap |
|  | Sponsor: | University of Auckland |
|  | Clock Start Date: | 12 April 2018 |

Dr Patrick Yap was present by teleconference for discussion for some of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The Researcher(s) propose trio whole exome sequencing in patients with genetic conditions undiagnosed after comprehensive genetic testing, and those with unique phenotypes, for which the genetic causes are unknown.
2. The sequencing and data analysis will be performed by Professor Stefan Bohlander and Dr Purvi Kakadiya from University of Auckland (Leukemia and Blood Cancer Research Unit). The clinical interpretation of results will be done through Genomic multidisciplinary meeting led by Dr Patrick Yap.

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 how the sequencing diagnoses rare diseases, adding that it was possible to uncover other general previously undiagnosed diseases too
2. F.1.2, P.4.1 and p.4.2 – The Committee felt that comments on Maoridom were rather patronising and rude. Please reconsider these responses for future applications.

Summary of ethical issues (outstanding)

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

1. There was a reviewer question about the disease focus and patient selection processes. Please explain how the researchers addressed this.
2. P.3.2.1 – states that researchers will seek guardians’ consent for adults who cannot provide their own consent, and that the participant information sheet mentions ‘dependents’.
3. The Committee stated that it is not possible for HDECs to approve an application unless it is consistent with New Zealand law, including the right not to be subjected to medical or scientific experimentation without that person's consent (section 10 of the New Zealand Bill of Rights Act 1990). Research involving participants who are not competent to consent is inconsistent with the Bill of Rights unless it is undertaken in accordance with Right 7(4) of the of the Code of Health and Disability Services Consumers’ Rights.
4. Please note that The Committee notes that proxy consent is only legally acceptable in cases where there is no medical experiment or if there is a medical experiment its purpose was tosave the person’s life or prevent serious damage to the person’s health.
5. The Committee has not considered this study to be seeking involvement of adults who cannot consent as the ethical standards and legal conditions for such involvement have not been outlined and addressed. Please remove mention of inclusion of adults who cannot provide their own consent and confirm that this has been done in writing to the Committee.
6. Please provide suitable information sheets and assent forms. This includes an information sheet and consent form for parents of participants unable to provide informed consent, an information sheet and consent form for participants able to provide their own informed consent (this includes all participants aged 16 years or older and may include some younger participants if they are deemed competent), an information sheet and assent form for children, and a very simple information sheet and assent form for young children that should very simply explain their participation in the study. Guidance on assent can be found at <https://ethics.health.govt.nz/guides-templates-forms-0>
7. Please submit diagrams that will be used for school age children.
8. Please explain how the study has considered development of Maori researchers (from the peer review).
9. The Committee noted that the application states that results will be reported in a way that does identify participants. Is this an error? If not, please explain why this is necessary.
10. Please clarify future testing of tissue and subsequent storage. Is this specific or for the study explicitly. If it is unspecified research lease provide a separate Participant Information Sheet and Consent Form for the use of tissue for future unspecified research that meets the *Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes).*

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

1. The Committee noted that the opening sentence of participant information sheet was confusing. The Researcher(s) explained what they meant by ultra-rare undiagnosed condition. The Committee requested that the researchers please reconsider the language used to describe an undiagnosed genetic condition.
2. Please consider whether the consent form yes or no options are truly optional. If they are not optional remove the tick box.
3. Consent has repeated items – please review and remove those that are not required.
4. On page 4 of the participant information sheet it states that insurance will not be affected. The Committee noted that this should be removed as this cannot be guaranteed with genetic information.
5. The Committee requested the compensation wording is updated for accuracy, they suggested the following statement: *“If you were injured in this study, which is unlikely, you would be eligible* ***to apply*** *for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery. If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.”*

Decision

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

* Please amend the information sheet and consent form, and assent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Observation Studies* *para 6.11*).
* Please provide age appropriate assent form for non-consenting (children) participants to sign (*Ethical Guidelines for Observation Studies 6.21)*
* The study design must minimise risk of harm. Address privacy concerns outlined by the Committee. (*Ethical Guidelines for Observation Studies* *para 5.5*).
* Confirm that the study does not involve non-consenting participants. (Ethical Guidelines for Observational Studies para 6.20).

This following information will be reviewed, and a final decision made on the application, by Dr Peter Gallagher and Dr Cordelia Thomas.

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| **5** | **Ethics ref:** | **18/CEN/63** |
|  | Title: | QoL preferences in CRC patients aged 80+ |
|  | Principal Investigator: | Dr Andrew McCombie |
|  | Sponsor: |  |
|  | Clock Start Date: | 12 April 2018 |

Dr. Andrew McCombie 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. Colorectal cancer (CRC) occurs often in the elderly. Approximately 12% of people newly diagnosed with CRC are aged 84 or older. With the population of New Zealanders aged 85 and over projected to rise from 83,000 in 2016 to 239,000-284,000 in 2043, the prevalence of CRC among the elderly will increase significantly. However, the elderly are underrepresented in clinical trials.
2. Little is known about quality of life (QoL) of CRC patients aged 80 and older. Moreover, QoL studies to date have not canvassed the opinions of 80+ year olds in terms of what they consider to be important regarding their survival and have assumed they put the same weight on the various factors as younger patients do. This may not be the correct approach. For example, a study comparing 60-79-year olds to 80+ year olds revealed that younger patients regarded eight domains to be more important, namely QoL, freedom from pain, feeling happiness/enjoyment in life, feeling content, ability to take care of activities of daily living, ability to work, home environment, and adequate social help.
3. This study will use mixed methodology and the primary aim is to determine what factors CRC patients aged 80 and older consider important in terms of survivorship.

Summary of ethical issues (resolved)

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

1. The Committee asked whether a support person could be available during the interview. The Researcher(s) confirmed there was.
2. The Researcher(s) confirmed that the interviews will be in a private location in the hospital.
3. The Researcher(s) explained participants will be recruited from hospital. The Committee noted that 30 minutes would not be long enough to cover all of the questions, particularly with this patient population. The Researcher(s) stated happy to change to 45 minutes. The Committee noted it could take up to 90 minutes.
4. The Committee queried why the researchers were not using a validated questionnaire, for example the highly validated EORTC CR29 for colorectal patients. The Researcher(s) confirmed used this questionnaire previously. The Researcher(s) concerns were that it does not ask the patients how important these symptoms were to them, adding some symptom would be more important than others to different age groups.
5. The Committee queried whether this was a pilot study for developing a new questionnaire. The Researcher(s) confirmed that the end goal is to develop a questionnaire, but that this is not an outcome for this study. The reason why existing questionnaires are not fit for purpose is because the aim is to have QoL more specifically for appropriateness for surgery, adding that no one has asked people of this age group what they think of surgery, and why they want to do it or expect to get out of it.
6. The Researcher(s) explained participants are those who have not had surgery yet. When recruited, the participants would have been diagnosed with CoC but not had surgery.
7. The Committee asked why there was an emphasis on surgery, with no space allocated for questions about chemotherapy or radiation therapy. The Researcher(s) explained that the study was driven by surgeons with an obvious focus on surgery. The Committee felt that the other two treatment options would also affect their quality of life and needed to be considered.

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 raised concerns about how the various questions were worded and finishing the interview with the final question. This particular question may be emotionally loaded for these patients, particularly for those who look after an elderly spouse. There needs to be a greater level of sensitivity to the wording of those questions. The Researcher(s) explained that they had not thought of it from that angle. The Researcher(s) explain that surgeons were interested in those kinds of questions but understand the Committee point of view. The Committee asked for more consideration around the order and type of questions asked.
2. The Committee suggested similar questions are asked about chemotherapy and radiation therapy as well, as these also impacts QoL.
3. Please make it clear that interviews will be recorded, transcribed and consider whether participants will have an opportunity to review their transcripts.
4. The Committee queried the peer review, noting the patient population. Perhaps it would be helpful to seek review from someone with more expertise in this patient group, such as a Geriatrician. This is a suggestion, which may add value to study. The Committee explained that this is about the cohort, as well as colorectal cancer.

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

1. The Committee requested the compensation wording is updated for accuracy, they suggested the following statement: *“If you were injured in this study, which is unlikely, you would be eligible* ***to apply*** *for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery. If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.”*
2. Remove ‘I consent to GP’ and ‘significant abnormal results’.
3. Please give an example of ‘questions of a sensitive nature’.
4. Remove sentence about interpreters, as you have stated there is no money for this service.

Decision

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

* Please amend the information sheet, consent form, and interview schedule, taking into account the suggestions made by the Committee (*Ethical Guidelines for Observation Studies* *para 6.11*).

This following information will be reviewed, and a final decision made on the application, by Dr Patries Herst and Mrs Helen Walker.

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| **6** | **Ethics ref:** | **18/CEN/64** |
|  | Title: | Study to Evaluate the Efficacy and Safety of VIS410 in Addition to Oseltamivir Compared with Oseltamivir Alone in the Treatment of Influenza A |
|  | Principal Investigator: | Dr James Taylor |
|  | Sponsor: |  |
|  | Clock Start Date: | 12 April 2018 |

Dr James Taylor 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 main aim of this study is to evaluate the effect of 2 dose levels of VIS410 + oseltamivir (Tamiflu) on the time to normalization of respiratory function compared to oseltamivir alone. Safety and tolerability will also be assessed.
2. Approximately 390 participants who meet the eligibility criteria will be randomized to 1 of three treatment groups (VIS410 2000 mg + Oseltamivir, VIS 4000 mg + Oseltamavir and matching placebo + Oseltamavir) at a ratio of 1:1:1.
3. Following 50% enrolment (190 participants) an interim analysis may be conducted, by an unblinded third party to assess if one of the VIS410 treatment arms can be terminated early for futility. A pre-specified sample size reanalysis may also be conducted based on the observed effect size. The interim analysis may also test the primary efficacy objective to assess if the primary efficacy endpoint has been met. If the VIS410 effect size proves to be greater than anticipated, then it is possible that the primary study endpoint will be met by the time the interim efficacy analysis is performed. In the event the interim analysis reveals that the primary efficacy endpoint has been satisfied, this Phase 2 study could be terminated for efficacy.
4. There will be up to 8 clinic visits - Screening, Day 1 (Baseline, Predose, 0 Hour, End of Infusion), and Days 3, 5, 7, 14, 28, 56. Study Assessments will be conducted at each visit.

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 the recruitment and consent process, noting that the Researcher(s) go through the participant information sheet with potential participants verbally due to its complexity.
2. The Researcher(s) noted that the pharmacist is unblinded.
3. The Committee commended the tables in the participant information sheet.
4. The Committee queried the Maori statistics in the application form P.4.1. The Researcher(s) responded that they think by extrapolation, that Maori are at higher risk for complications from influenza, i.e. from other native populations (aborigines, native Americans), but do not think Maori are more likely to get infection, rather more likely to get severe infection, due to socioeconomic circumstances.
5. Page 26 of application states ‘Maori will be given same opportunity’. The Committee noted that this should be a given. The Researcher(s) agreed. The Committee noted for future reference that this section is about cultural issues, for example the head, having whanau around them or experiencing whakama about being sick.

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 about recruitment. The Researcher(s) explained recruitment will occur in the wards of hospital and will be split between medical wards and the medical high dependency unit, adding it was possible for participants to be in ICU. The Researcher(s) explained that the study is not specifically recruiting ventilated patients, as this study does not have robust enough data about this drug, to give to just anyone who has flu.
2. The Committee stated that it is not possible for HDECs to approve an application unless it is consistent with New Zealand law, including the right not to be subjected to medical or scientific experimentation without that person's consent (section 10 of the New Zealand Bill of Rights Act 1990). Research involving participants who are not competent to consent is inconsistent with the Bill of Rights unless it is undertaken in accordance with Right 7 (4) of the of the Code of Health and Disability Services Consumers’ Rights.
3. Please note that The Committee notes that proxy consent is only legally acceptable in cases where there is no medical experiment or the purpose of the medical experiment is to save the person’s life or prevent serious damage to the person’s health.
4. The Committee has not considered this study to be seeking involvement of adults who cannot consent as the ethical standards and legal conditions for such involvement have not been outlined and addressed. Please remove mention of inclusion of adults who cannot provide their own consent and confirm that this has been done in writing to the Committee.
5. The Researcher(s) explained process of identifying when someone was too unwell to participate. The Committee noted this.

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

1. Page 7 states participants may directly benefit by receiving treatment from study drug which is unavailable in New Zealand. This infers that it is a benefit to get the drug, which is unknown at the moment. Please remove the word “directly”.
2. Page 19 - legally authorised representatives. Please remove this and any mention of legally authorised representatives.
3. The Committee asked for clarification about the pregnancy outcome measures. The Researcher(s) explained they wanted to access medical records. The Committee required an ‘access to medical information bullet point’, and clarify what information is collected, noting information about the child must only be collected once child is born live.
4. The Committee noted there are triple negatives used – this is unnecessarily confusing. Please review.
5. The Committee noted the requirement telling the pregnant partner to tell her partner to keep on contraceptives. This could be removed.
6. Add contact details for support groups and Maori – see template participant information sheet for guidance <https://ethics.health.govt.nz/guides-templates-forms-0>

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).
* Confirm that the study does not involve non-consenting participants. (Ethical Guidelines for Intervention Studies para 6.26-6.28).

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

|  |  |  |
| --- | --- | --- |
| **8** | **Ethics ref:** | **18/CEN/65** |
|  | Title: | M14-728 R/R Chronic Lymphocytic Leukemia |
|  | Principal Investigator: | Dr Sean MacPherson |
|  | Sponsor: | AbbVie Pty Ltd |
|  | Clock Start Date: | 12 April 2018 |

Dr Sean MacPherson was not present for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The primary aim is to evaluate the overall response rate of venetoclax monotherapy in participants with relapsed or refractory chronic lymphocytic leukemia (CLL) in the presence of 17p deletion. The secondary aims are to evaluate the complete remission rate, partial remission rate, progression free survival, event free survival, time to progression, time to 50% reduction in absolute lymphocyte count, overall survival and percent of subjects who move on to stem cell transplant. The safety and tolerability of venetoclax in participants with relapsed or refractory CLL in the presence of 17p deletion will also be evaluated.
2. Approximately 70 patients with relapsed or refractory CLL in the presence of 17p deletion will be recruited from Australia, New Zealand, China mainland and Taiwan.
3. Patients will be identified with the 17p deletion and screening procedures will take place. Participants will receive venetoclax with a starting dose of 20mg; a ramp up will proceed weekly up to 400mg as tolerated.

Summary of ethical issues (outstanding)

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

1. The Committee noted that there were unclear and conflicting statements regarding use of tissue, biobanking and future unspecified research. Please provide clear information about what tissue use is involved, what sub or optional studies are available and any biobanking. The Committee noted that question O and B.4.5 indicate that there is no future unspecified research, however within the participant information sheet it stages “AbbVie and people or companies working with AbbVie may use your biological samples when developing new tests, procedures and commercial products. If this happens, AbbVie does not plan to share any profits with you.” on page 12. This is future unspecified research and would require a separate participant information sheet and consent form.
2. The Committee asked what restrictions are placed on publication. Please explain in a cover letter.
3. P.4.1 – please readdress the question in a cover letter covering benefits for Maori.
4. F.1.2 – any statistics available, if so please advise the Committee.

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

1. Add that study drug is not funded but is approved in New Zealand.
2. Add more recent information on number of people who have had treatment or been exposed to it. Current data is from November 2016.
3. Page 2 – please make it clearer as to whether compassionate supply will be available will be available at the completion of the study.
4. The Committee appreciated the table however asked if it is possible to condense it, perhaps by removing the notes to improve readability.
5. There is lots of repetition. Please revise.
6. Page 20 – The Committee asked why the study limits access to health records when the study is open label. There is no requirement for blinding and therefore should be no restrictions on access to participants own records.
7. Pregnancy participant information sheet – add Maori support details and researcher details and ensure consent for child data is sought after baby is born.
8. Page 3 – consent form – states participants must ask study doctor to know what diseases tested for? This should be a study doctor obligation not participant obligation.
9. Change ‘Will follow up’ to ‘will ask to follow up’ with regards to unexpected pregnancy, and it should refer to the pregnancy participant information sheet, not refer to ‘this’ participant information sheet
10. Please review all medication – Page 11 – this should also not be a participant obligation but a study doctor obligation.
11. Change to ‘your study drug’ from ‘the study drug’.
12. Male partner sterilisation – is not included as an acceptable means of contraception. Please clarify.
13. The Committee noted that there are confusing brackets and lots of jargon, especially around the lists of potential side effects. Please explain or delete jargon.
14. Page 21- paragraphs on test samples and cultural considerations are under the subheading – ‘what happens if I change my mind’. Please ensure sections are under appropriate subheadings.
15. Add limitation on travel reimbursement or define reasonable.

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 address how the study may benefit Māori and how cultural issues that may arise for Māori participants in the study will be managed (*Ethical Guidelines for Intervention Studies* *para 4.7*).
* Explain use of tissue in a cover letter.
* If future unspecified research is occurring, please provide a separate Participant Information Sheet and Consent Form for the use of tissue for future unspecified research. (*Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes, para 2*).

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

|  |  |  |
| --- | --- | --- |
| **9** | **Ethics ref:** | **18/CEN/67** |
|  | Title: | Topical Timolol Treatment of Superficial Proliferating Infantile Haemangioma |
|  | Principal Investigator: | Dr Swee Tan |
|  | Sponsor: | Gillies McIndoe Research Institute |
|  | Clock Start Date: | 12 April 2018 |

Dr Frederica Steiner 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.

Dr Dean Quinn declared a potential conflict of interest, and the Committee decided to have Dr Quinn remain in the room but not participate in the decision of the application.

Summary of Study

1. The study aims to show that topical timolol is an effective, safe, and well tolerated treatment for superficial strawberry birthmarks.
2. Infantile haemangioma (IH) is the most common benign tumour of infancy, affecting 4-10% of children with a preponderance for female, Caucasian, and premature infants. propranolol is now the mainstay treatment for problematic proliferating IH. Multiple studies have shown the effectiveness of topical propranolol and topical timolol for the treatment of superficial IHs with minimal side effects.
3. Timolol maleate is a topical β-blocker that has been used for the treatment of glaucoma in the paediatric population for over 30 years. Most IHs do not require active treatment as they involute spontaneously over time. However, up to 10-15% of IH require intervention during infancy because they cause complications, such as visual and airway obstruction, ulceration, bleeding, and permanent disfigurement.
4. With this study the Researcher(s) hope to find an improved way of treating IHs with potentially less side effects.

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 peer review was not signed.
2. Queried Maori prevalence, is it prevalent or not? Irrespective of this, Maori consultation is required. Noted this has been sought.
3. The Researcher(s) confirmed photos were discussed in the participant information sheet.
4. The Researcher(s) confirmed will not have any identifiable pictures, in presentations etc.
5. The Committee asked who the sponsor was for this study. The Researcher(s) explained that the study is run through DHB clinic.
6. P.4.2 – please answer this question with respect to cultural issues, in future applications.

Summary of ethical issues (outstanding)

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

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

1. Page 2, The Committee suggested another potential benefit is that birthmarks may improve.
2. Add contact details for HDEC at the end. See template participant information sheet for guidance <https://ethics.health.govt.nz/guides-templates-forms-0>
3. Please add details on low blood pressure – examples of symptoms that they would be concerned about,
4. The Committee asked about the evidence base for the treatment. The Researcher(s) stated they not know what proportion of participants it does work for. Current evidence is based on a number of small case series, as well as practitioners who do use it, seemingly with positive effects. The Committee noted it should be reworded that ‘recent studies show it may be effective, not that is effective’.
5. Layout for participant information sheet – most of the content is in it but the current structure and layout is confusing. Please review the template participant information sheet for suggestions on layout and order.
6. Please make sure side effects are part of participant information sheet not appendix 3.
7. The Committee noted if people do not apply the treatment properly results will be impacted. Add ‘my participation’ as parents applying the gel – make it clear how to use it.
8. Detail in the participant information sheet but also a separate laminated sheet with how to respond to any adverse events, what to look for and the numbers to call.
9. The Researcher(s) stated confirmed GP notification was mandatory for this study. The Committee requested that therefore the participant information sheet explains rights and record access, GP and auditors, in this section.

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 Dr Cordelia Thomas and Dr Melissa Cragg.

|  |  |  |
| --- | --- | --- |
| **10** | **Ethics ref:** | **18/CEN/68** |
|  | Title: | Near infrared imaging of amputated limbs |
|  | Principal Investigator: | MS. Jo Krysa |
|  | Sponsor: |  |
|  | Clock Start Date: | 12 April 2018 |

Ms Kari Clifford 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. Chronic venous insufficiency (CVI) in some patients can lead to varicose veins, pain, venous ulceration, and loss of limb. To date, it is not possible to predict in which patients with CVI the disease will progress. Previously the Researcher(s) have shown that venous insufficiency can be present in the microvenous network, even when ultrasound diagnostics show that the great saphenous vein (GSV) has no reflux. Previous work by our group in a pilot study suggested that microvenous structures can be imaged with a near-infra red camera, and this study is a continuation of that work.
2. The Researcher(s) aim to investigate microvenous vessels and their abnormalities using near infrared imaging (NIR) by correlating NIR data with observable venous structures in resin casts of amputated limbs.
3. Participants (6) will be chosen from patients at the Dunedin Hospital awaiting a limb amputation. This study employs a descriptive correlational design involving three components.
4. One amputated lower limb will be frozen for 24 hrs, then thawed and imaged with a venogram, and a near-infra red (NIR) camera and indocyanine green dye contrast. After imaging and an angiogram, limb will undergo resin casting, whereby resin will be injected into veins of the limb and allowed to set. The resulting resin map will be analysed to determine the degree of venous reflux in the limb. This will be correlated with the data obtained from the NIR imaging and the angiogram. This first frozen limb is a test of the feasibility of freezing. If not feasible, subsequent limbs will be imaged within 24 hours of amputation. Two more limbs will be studied to determine whether discernible images can be obtained.
5. If part one provides usable data from both imaging and resin casting, participants will be asked if they would like to undergo imaging prior to amputation, to allow for better correlation. We aim to have three more participants, with at least one who is able to undergo imaging prior to amputation.

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 if patients are well known to the study team. The Researcher(s) confirmed they were, with scheduled amputation.
2. The Researcher(s) explained criteria for being eligible, particularly must be unable to feel pain. This is decided by surgeon who is not part of the study.
3. The Researcher(s) confirmed that the three participants who have the dye are not the same people who would have resin mapping.

Summary of ethical issues (outstanding)

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

1. Anaphylactic and vascular reactions in to a history with allergy – this should be an exclusion criterion. The Researcher(s) acknowledged this and would ask doctors involved.

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

1. The Committee asked if participant information sheet can be written to be a bit warmer, or the preamble could be a bit longer – effectively more clarity regarding why the study is being done.
2. Current wording implies that amputation is part of the study, however it is actually why they are part of the study.
3. Make it clearer about use of limb post-amputation.
4. More generally, please see template participant information sheet for guidance on format and content, including ACC information <https://ethics.health.govt.nz/guides-templates-forms-0>
5. Add contact numbers for Maori support, HDEC and HDC etc. – see template.
6. The Committee noted that while the consent states can withdraw at any time – it should note what can and can’t be withdrawn at different time points, for example cannot withdraw after procedure, at which point it is about withdrawing data.
7. Review for typos.
8. The Committee noted participant information sheet implies that they could not be neuropathic, but the Researcher(s) confirmed that they must be neuropathic. Please clarify this in the participant information sheet.
9. Notification of GP – this should be in information sheet and consent form.
10. Revise the yes/no statements on the consent form and only have those as an option if 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 forms taking into account the suggestions made by the Committee (*Ethical Guidelines for Observation Studies* *para 6.11*).
* Confirm exclusion criteria (*Ethical Guidelines for Observation Studies* *para 5.5*).

This following information will be reviewed, and a final decision made on the application, by Dr Peter Gallagher and Mrs Helen Walker.

|  |  |  |
| --- | --- | --- |
| **11** | **Ethics ref:** | **18/CEN/69** |
|  | Title: | HART cohort linkage to National Mortality Record Data |
|  | Principal Investigator: | Dr Joanne Allen |
|  | Sponsor: |  |
|  | Clock Start Date: | 12 April 2018 |

Dr Joanne Allen was present in person for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The project involves linkage to records held by the Ministry of Health (MoH) for participants in the New Zealand Health, Work and Retirement longitudinal cohort study, conducted by the Health and Ageing Research Team (HART; Massey University). The longitudinal study commenced in 2006 with the recruitment of a cohort of adults aged 55-70 years. Additional participant cohorts are recruited to the study every 2-3 years. Participants are randomly selected from the New Zealand electoral roll and approached to participate in the postal survey. Respondents are re-surveyed on a biennial basis.
2. Participant mortality outcomes represent important data in identifying predictors of participant health. Additionally, this information enables researchers to account for study attrition rates due to mortality. Confirmation of mortality status prior to each survey wave is an activity supported by the HART Data-Linkage Advisory Panel and was proposed by the Massey University Human Ethics Committee as an aid to prevent potential anguish to the families of deceased participants which may occur when researchers attempt to contact non-responding participants.
3. The research activity involves providing the MoH with an ID key and minimum identifying information (i.e., name, sex, dob) required for the Ministry of Health to match these details to a NHI number. The NHI number is then separated from minimum identifiers and matched to participant mortality status and cause of death. The NHI number is then also removed and mortality information communicated to the Health and Ageing Research Team.
4. The minimum identifiers provided to the MoH by the study reflect the same information that all New Zealanders provide for inclusion on the New Zealand Electoral Roll. At no time will the MoH have access participant data or information regarding their participation status. This research activity has previously been approved by the Central HDEC (14/CEN/79, dated 26 June 2014, expired 26 June 2017).

Summary of ethical issues (resolved)

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

1. The Committee understood why the first data linkage was sought, and why HDEC granted it. However, the Committee queried why consent is not sought at the time when continual enrolment is not sought at the time of new recruitment. The Researcher(s) explained that people who are recruited from 2016 onwards are approached for data linkage. The Researcher(s) stated mortality linkage was not sought due to the waiver. However, the waiver study (HDEC application 14/CEN/79) had expired. The Committee noted that that 14/CEN/79 had also failed to submit any annual progress reports or final repots and had received numerous reminders about this. The application was not compliant with HDEC requirements. Please submit progress reports about this study to the HDEC, in order to provide context, and also potential benefit, in order to support the application before HDEC about mortality data.
2. The Committee explained that a waiver is an exception to the rule, not an institutionalised norm. The Committee explained history of consent and mechanism of the waiver, including the arguments and considerations that must be made by the researchers and considered by the HDEC.
3. The Committee asked if consent can be sought to data link, going forward with future surveys.
4. The Committee asked what percent are able to keep in touch every 2-3 years. The Researcher(s) responded about 79%. Often non-responders have died, but not necessarily.
5. The Researcher(s) explained that the waiver is both a practical need but also an important study outcome (scientific merit).
6. The Committee noted if the Researcher(s) sought consent from 80%, could the waiver be limited to those who were lost to follow up.
7. The Researcher(s) clarified – project started in 2006. Initiated data link process in 2013. Predated IDI. New process developed. At that point, applied for mortality data link, under different application 14/CEN/79. This is because could not seek consent for mortality for that study. Written consent sought for health data linking in future surveys (but not mortality data, still). Approached people 2014/15. In 2016 – request written consent for data link again.
8. The Committee explained expectations around participants, in terms of what they consented to, is helpful to give context in granting a waiver. Please provide the HDEC with the participant information sheet that would have been used by participants.
9. The Committee note scientific need to access mortality records, for reasons of undue anxiety.
10. The Committee noted going forward new (2018) should seek permission for morality. If some further information is provided to HDEC (listed below) the HDEC will consider the waiver for the most recent rounds, on the view that going forward consent is sought for mortality linkage, including in 2018.
11. The Researcher(s) stated major scientific methodology issues if not able to link.
12. The Researcher(s) explained that this is a very unique data set. The study will continue to 2020, with significant public benefit and lots of publication(s).

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 progress reports for the study to date.
2. The Committee requested prior participant information sheets.
3. The Committee requested scientific review on the data linkage, in order to demonstrate harm reduction.
4. The Committee requested Maori consultation evidence.
5. The Committee requested a plan and or thinking around consent going forward.

Decision

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

The Committee noted that they can approve access to identifiable health information without consent for research in certain circumstances. The Ethical Guidelines for Observational Studies states at Paragraph 6.43:

* 1. *Access to identified or potentially identifiable data for research without the consent of the people the data identifies or makes potentially identifiable may be justifiable when:*
     1. *the procedures required to obtain consent are likely to cause unnecessary anxiety for those whose consent would be sought; or the requirement for consent would prejudice the scientific value of the study; or it is impossible in practice to obtain consent due to the quantity or age of the records; and*
     2. *there would be no disadvantage to the participants or their relatives or to any collectives involved; and*
     3. *the public interest in the study outweighs the public interest in privacy.*

To approve a study involving access to health information without consent the Committee must be satisfied that these requirements are met by the study concerned.

This following information will be reviewed, and a final decision made on the application, by Mrs Helen Walker and Dr Dean Quinn.

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| **12** | **Ethics ref:** | **18/CEN/71** |
|  | Title: | A study assessing the similarity of Actemra®, RoActemra® and the trial drugLusiNEX. |
|  | Principal Investigator: | Dr Chris Wynne |
|  | Sponsor: | Quintiles Pty Limited |
|  | Clock Start Date: | 12 April 2018 |

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. Tocilizumab is used for the treatment of moderate to severe rheumatoid arthritis (RA). The sponsor has developed a drug similar to tocilizumab, called LusiNEX. This study aims to test that LusiNEX is similar to US licensed Actemra and the EU approved RoActemra.
2. The study will also compare drug safety, how well it is tolerated, the levels of the drug in the blood at different times, and the body's immune response. It will also evaluate the change in absolute neutrophil count, c-reactive protein, and soluble interleukin-6 receptor (sIL-6R).
3. Up to 190 healthy male and female subjects who meet the required entry criteria will be randomly assigned to one of the three treatment groups in a 1:1:1 ratio to receive a single intravenous transfusion 4mg/kg dose of either LusiNEX, Actemra® or RoActemra®.
4. The study requires a two-night inpatient stay and eleven outpatient visits.
5. The results will be used to further develop LusiNEX as a biosimilar to tocilizumab.

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 the context for this study, noting they had recently completed a very similar study.
2. The Committee and the Researcher(s) discussed the statistics and context of p.4.1 of the application.
3. P.4.2 – The Committee noted the wording, that it was important for Maori to understand fully, is a bit patronising. The Researcher(s) noted they would take this feedback on board.

Summary of ethical issues (outstanding)

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

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

1. Please explain what counts as a social smoker.
2. The Committee noted there is no general legal requirement for clinical trials to receive ethics approval.
3. Page 10 if woman who is pregnant or intend to become pregnant. Clarify whether this means ever or during the study.
4. In future please consider an amendment to have a separate participant information sheet for pregnant partners.

Decision

This application was *approved* by consensus, with nonstandard conditions.

|  |  |  |
| --- | --- | --- |
| **13** | **Ethics ref:** | **18/CEN/72** **(CLOSED)** |
|  | Title: | Assessment of JUUL 1.7% AND 5% Nicotine Salt Based ENDS Products, when Used by healthyadult smokers. |
|  | Principal Investigator: | Dr Chris Wynne |
|  | Sponsor: | JUUL Lab Inc |
|  | Clock Start Date: | 12 April 2018 |

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. JUUL Labs, Inc is a private company founded to develop alternatives to traditional cigarette smoking. The company uses vaporisation and "heatnotburn" technologies for the inhalation of nicotine, so that burning is avoided, and vapour rather than smoke is generated.
2. These products may be an acceptable alternative to traditional smoking, as the generation and inhalation of smoke, tar and carbon monoxide can be avoided.
3. In particular the researchers want to know:

* How much nicotine gets into the blood with each product?
* How quickly does nicotine reach maximum levels in the blood with each product?
* The change in exhaled carbon monoxide (CO) following administration of each product
* How satisfied are the users with each product?
* Approximately 24 healthy adult smokers will take part in the study.

1. Blood tests to measure nicotine levels will be taken at certain times for each product, and any side effects will be recorded. The results can then be compared. A questionnaire on satisfaction will be given after each product has been tested.
2. This study will provide the company with comparative information about nicotine levels of the Sponsor products and traditional cigarettes. Results will also be used to guide how participants may be asked to use the products in future clinical trials.

Summary of ethical issues (resolved)

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

1. P.4.2 – The Committee noted the wording, that it was important for Maori to understand fully, is a bit patronising. The Researcher(s) noted they would take this feedback on board.

Summary of ethical issues (outstanding)

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

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

1. Relate blood taken to comparative volume, for example blood donor amount in one sitting or number of soda cans.
2. Pg.8 of 10 – change STH to CEN.
3. 4 para down – what happen to my information. Medical files – medical files for the study or all medical files? The Researcher(s) stated only what happens in the study. Sponsor and monitors cannot look at files outside of that study.
4. Make bullets points reflect the wording; A to J.

Decision

This application was *approved* with one member abstaining.

## Review of approved studies

|  |  |  |
| --- | --- | --- |
| **1** | **Ethics ref:** | **17/CEN/229** - Amendment |
|  | Title: | (duplicate) ANZpHOD |
|  | Principal Investigator: | Dr Emma Best |
|  | Sponsor: |  |
|  | Clock Start Date: | 16 November 2017 |

Dr Emma Best was not present for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This application concerned a reconsideration of HDEC’s initial decision to require consent from participants. The Researcher(s) submitted a letter that made a case for not seeking consent.

Summary of ethical issues (resolved)

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

1. The Committee note cannot try other method till come back. Invite to resubmit back. Decline!

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 parental consent can only be provided for participants under 18. The Committee noted adults cannot have their parents make decisions for participant in research.
2. The Committee also noted at no point did they suggest the recruitment method outlined in the letter, leading to the risks outlined in the letter.
3. The Committee stated that although there are exceptions to seeking consent to use information, in light of sensitivity of this data and in light of the ability to contact these people, the researchers must devise a way to contact those participants that mitigates the risks outlined by the letter provided by the researchers. There are ways to seek permission that involve reducing risks of harm.
4. The Committee referred to the requirements to accessing health information without consent. The three requirements are not all met, while the public interest in the study is high, it is not yet proven to be impracticable to have a procedure that cannot avoid anxiety, or that there are sufficient numbers of participants that mean it is not possible to seek consent.
5. A range of options are available, including generic letter, telephone calls with generic information not specific, or through GPs.
6. The letter could generally be about research, and health information in order to increase participation involve one phone call (which does not disclose any HIV status etc., and before doing any such disclosure, and confirms that it is the person that is being recruited).

Decision

This amendment was *declined.*

The Committee noted that they can approve access to identifiable health information without consent for research in certain circumstances. The Ethical Guidelines for Observational Studies states at Paragraph 6.43:

1. *Access to identified or potentially identifiable data for research without the consent of the people the data identifies or makes potentially identifiable may be justifiable when:*
   * 1. *the procedures required to obtain consent are likely to cause unnecessary anxiety for those whose consent would be sought; or the requirement for consent would prejudice the scientific value of the study; or it is impossible in practice to obtain consent due to the quantity or age of the records; and*
     2. *there would be no disadvantage to the participants or their relatives or to any collectives involved; and*
     3. *the public interest in the study outweighs the public interest in privacy.*

To approve a study involving access to health information without consent the Committee must be satisfied that these requirements are met by the study concerned. The study team has not made a compelling argument that means that the procedures required to obtain consent are likely to cause anxiety or harm.

## General business

1. The Committee noted the content of the “noting section” of the agenda.
2. 18/CEN/37 – noted response was due and requested HDEC members to review.
3. The Chair reminded the Committee of the date and time of its next scheduled meeting, namely:

|  |  |
| --- | --- |
| **Meeting date:** | 22 May 2018, 08:00 AM |
| **Meeting venue:** | Room GN.6, Ground Floor, Ministry of Health, 133 Molesworth Street, Wellington, 6011 |

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 5.00pm