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| **Committee:** | Central Health and Disability Ethics Committee |
| **Meeting date:** | 22 January 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 |
| 12:05pm | Confirmation of minutes of meeting of 17 December 2018. |
| 12:30pm | 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  5:05-5:30 | i 18/CEN/262  ii 18/CEN/265  iii 18/CEN/264  iv 18/CEN/266  v 18/CEN/267  vi 18/CEN/263  vii 18/CEN/268  viii 18/CEN/279  ix 18/CEN/275  x 18/CEN/276  xi 19/CEN/4  xii 18/CEN/282 |
| 5:30pm | 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 | Apologies |  |
| 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 | Apologies |  |
| 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 |  |
| Mrs Helen Davidson | Lay (ethics?) | 06/12/2018 | 06/12/2021 | Present |

**Also in attendance:**

|  |  |  |
| --- | --- | --- |
| *Name* | *Position (or reason for attending)* |  |
| Mrs Leesa Russell | Co-opting |  |
| Ms Raewyn Iodine | Co-opting (Acting Chair) |

Welcome

The Acting Chair opened the meeting at 12:00 and welcomed Committee members, noting that apologies had been received from Mrs Helen Walker and Dr Dean Quinn.

The Acting Chair noted that it would be necessary to co-opt members of other HDECs in accordance with the Standard Operating Procedures. Mrs Leesa Russell confirmed her eligibility, and was co-opted by the Acting Chair as a member of the Committee for the duration of the meeting.

The Acting 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 17 December 2018 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **18/CEN/262** |  |
|  | Title: | A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Two-Arm, Phase 2 Study of ME-401 in Subjects with Follicular Lymphoma After Failure of Two or More Prior Systemic Therapies |  |
|  | Principal Investigator: | Dr Henry Chan |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 10 January 2019 |  |

Dr Chan was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This is a phase-2 study for patients who have Follicular Lymphoma and have already undergone 2 or more prior lines of treatment, which in most cases means the patient does not have any other standard of care available. The study will test ME-401, a new oral medication. Similar drugs have been tested in similar lymphoma and also follicular lymphoma before, and have been shown to be efficacious, however there are some issues of toxicity. For this reason, the study will initially involve daily treatment for all patients, followed by a randomisation to either continuous or intermittent treatment, to test whether intermittent treatment will be better tolerated and maintain the same efficacy.

Summary of resolved 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 for future reference, in answering question p.4.1 it would be helpful to provide statistics regarding the prevalence of this disease in Maori.
2. For future reference the Committee also stated that the Treaty of Waitangi is not a sufficient justification for research, as used to answer question f.1.2.

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

1. In the Pregnant Partner Participant Information Sheet/Consent Form, please amend the first two paragraphs to address not only the situation of a pregnant partner but also that of the participant becoming pregnant herself. Please include a schema of the study, including the blinding and unblinding options in the study in all Participant Information Sheets, such as that included in the protocol.
2. On page 7 of the main Participant Information Sheet under the heading ‘ME-401 Administration’, please indicate that the participant may continue to receive the drug *indefinitely* if they are tolerating it well and if the drug keeps their lymphoma in check.
3. Please add to the main Participant Information Sheet and Consent Form that you will inform the health practitioner with responsibility for the participant’s primary care of their participation in the study.
4. 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 *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:** | **18/CEN/265** | |  |
|  | Title: | M16-047: Moderate to Severe Atopic Dermatitis: Evaluation of Upadacitinib in Combination with Topical Corticosteroids in Adolescent and Adult Subjects | |  |
|  | Principal Investigator: | Prof Marius Rademaker | |  |
|  | Sponsor:  Clock Start Date: | AbbVie  10 January 2019 | |  |
|  | | |  |

Reenu Arora was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The study aims to assess the efficacy and Safety of upadacitinib when used in combination with topical corticosteroids for the treatment of adolescent and adult subjects with moderate to severe atopic dermatitis who are candidates for systemic therapy. The co-primary endpoints are: the proportion of participants achieving at least a 75% reduction in Eczema Area and Severity Index (EASI 75) from baseline at week 16, and the proportion of participants achieving validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD) of 0 or 1 with a least two grades of reduction from baseline at week 16.

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 several issues regarding the inclusion of adolescents in the study and the justifiability of doing so. In particular, the following issues were of concern:   
     
   i. It is unclear how young people (from 12 years of age) will have ‘sexual activity’ explained to them  
   ii. If a child did become pregnant or is found to have HIV, this would need to be communicated to the parent, which should be clearly communicated to proposed participants  
   iii. Children may in many cases be able to provide informed consent, which would need to be individually assessed  
   iv. All documents would need to be amended to reflect the fact that participants are considered adults from 16 years of age and can provide full consent. As a result, children turning 16 during the study would need to re-consent  
   v. The Committee questioned the necessity of involving children in the study, especially noting the above difficulties.  
     
   For these reasons the Committee requested excluding adolescents, with the possibility of later applying to amend the study to include adolescents if desired. This was accepted by the researcher.

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 noted that several questions in the questionnaires could cause distress in some participants and strongly recommended that a safety plan would be in place to provide these participants with the support they need, such as providing phone numbers for or access to counsellors or psychologists.

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

1. Please ensure that all information regarding future unspecified use of the participants’ tissue is specific and consistent across all documentation.
2. Please remove the reference to “the flip of a coin” on page 2 (“a 50% chance” would be acceptable).
3. When mentioning the rescue therapy on page 2, it should be mentioned that not taking the therapy treatment may have other consequences, such as having to withdraw from the study.
4. Please state that individuals who do not take part in the first part of the study will be excluded from the extension period.
5. Please clarify in the main Participant Information Sheet whether the study will include inflammatory disease patients or not.
6. On page 10 of the main Participant Information Sheet and Consent Form it states that study data and samples may be shared with other companies. Please specify which companies the data or samples may be shared with.
7. The committee expressed that information regarding the optional research in the main Participant Information Sheet and Consent Form is not relevant to those participants. Please remove all references to the optional research.
8. Please amend any reference of a “spontaneous abortion” in the Pregnant Partner/Participant Information Sheet and Consent Form, referring instead to a “miscarriage”.

Decision

This application was *provisionally approved* by consensus for participants 16 years and older, subject to the following information being received:

* Please update the inclusion/exclusion criteria to exclude all participants under the age of 16 from this study (*Ethical Guidelines for Intervention Studies* paragraph5.30, point 2).
* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* paragraph6.22).
* Please create a safety plan in the case that any distress is detected in participantswhen answering the questionnaire documents, and update the Participant Information Sheet and Consent Forms to include that (*Ethical Guidelines for Intervention Studies* paragraph6.62).

This following information will be reviewed, and a final decision made on the application, by Mrs Leesa Russel and Ms Sandy Gill.

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| **3** | **Ethics ref:** | **18/CEN/264** |  |
|  | Title: | M16-045: Moderate to Severe Atopic Dermatitis: Evaluation of Upadacitinib in Adolescent and Adult Subjects |  |
|  | Principal Investigator: | Prof Marius Rademaker |  |
|  | Sponsor: | AbbVie |  |
|  | Clock Start Date: | 20 December 2018 |  |

Reenu Arora was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The study aims to assess the efficacy and Safety of upadacitinib for the treatment of adolescent and adult subjects with moderate to severe atopic dermatitis who are candidates for systemic therapy. The co-primary endpoints are: the proportion of participants achieving at least a 75% reduction in Eczema Area and Severity Index (EASI 75) from baseline at week 16, and the proportion of participants achieving validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD) of 0 or 1 with a least two grades of reduction from baseline at week 16.

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 several issues regarding the inclusion of adolescents in the study and the justifiability for doing so. In particular, the following issues were of concern:  
     
   i. It is unclear how young children (from 12 years of age) will have ‘sexual activity’ explained to them  
   ii. If a child did become pregnant or is found to have HIV, this would need to be communicated to the parent, which is a consequence the child may find difficult to fully understand  
   iii. Children may in many cases be able to provide informed consent, which would need to be assessed  
   iv. All documents would need to be amended to reflect the fact that participants are considered adults from 16 years of age and can provide full consent. As a result, children turning 16 during the study would need to re-consent  
   v. The Committee also questioned the necessity of involving children in the study, especially noting the above difficulties.  
     
   For these reasons the Committee requested excluding adolescents, with the possibility of later applying to amend the study to include adolescents if desired. This was accepted by the researcher.

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 noted that several questions in the questionnaires could cause distress in some participants and strongly recommended that a safety plan would be in place to provide these participants with the support they need, such as providing phone numbers for or access to counsellors or psychologists.

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

1. Please ensure that all information regarding future unspecified use of the participants’ tissue is specific and consistent across all documentation.
2. Please remove the reference to “the flip of a coin” on page 2 (“a 50% chance” would be acceptable).
3. When mentioning the rescue therapy on page 2, it should be mentioned that not taking the therapy treatment may have other consequences, such as having to withdraw from the study.
4. Please state that individuals who do not take part in the first part of the study will be excluded from the extension period.
5. Please clarify in the main Participant Information Sheet and Consent Form whether the study will include inflammatory disease patients or not.
6. On page 10 of the main Participant Information Sheet and Consent Form it states that study data and samples may be shared with other companies. Please specify which companies the data or samples may be shared with.
7. Please add contact details for the HDEC and Maori health support contact to the Pregnant Partner Information Sheet.
8. The Committee queried the lack of a Māori tissue statement in the Pregnant Partner Participant Information Sheet. Please use the same statement used on the other Participant Information Sheets, or similar.
9. The committee expressed that information regarding the optional research in the main Participant Information Sheet and Consent Form is not relevant to those participants. Please remove all references to the optional research.
10. The Committee pointed out that the Pregnant Partner/Participant Information Sheet and Consent Form was missing from the application. Please submit this.
11. Please state in the Participant Information Sheet and Consent Forms that the participant’s general or primary care practitioner will be informed of their participation in the study.

Decision

This application was *provisionally approved* by consensus for participants 16 years and older only, subject to the following information being received:

* Please update the inclusion/exclusion criteria to exclude all participants under the age of 16 from this study (*Ethical Guidelines for Intervention Studies* paragraph5.30, point 2).
* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* paragraph6.22).
* Please create a safety plan in the case that any distress is detected in participantswhen answering the questionnaire documents, and update the Participant Information Sheet and Consent Forms to include that (*Ethical Guidelines for Intervention Studies* paragraph6.62).

This following information will be reviewed, and a final decision made on the application, by Mrs Leesa Russel and Ms Sandy Gill.

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| **4** | **Ethics ref:** | **18/CEN/266** |  |  |  |
|  | Title: | DCR PHXC-201 - Study to Evaluate the Efficacy, Safety, and Tolerability of DCR PHXC Solution for Injection in Patients with Primary Hyperoxaluria |  |  |  |
|  | Principal Investigator: | Dr William Wong |  |  |  |
|  | Sponsor: | Pharmaceutical Solutions Ltd |  |  |  |
|  | Clock Start Date: | 20 December 2018 |  |

Dr William Wong 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 patient has a rare condition known as Primary Hyperoxaluria. This genetic condition results in the production of oxalate, which accumulates in various body organs, causing kidney stones and eventually kidney failure. Oxalate also accumulates in other organs and blood vessels, and has wide-ranging effects. The aim of this study is to assess a novel compound which is designed to direct the liver to produce less oxalate by tricking the liver into down-regulating and producing less oxalate. There is no other treatment available for this condition, so this is the first treatment available that can alter the cause of the disease.

Summary of resolved ethical issues

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

1. The Committee stated that for future applications with very few participants, it would be helpful indicate the ages and ability to consent of the participants.

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 noted that some of the questions in the questionnaires could cause distress, and that a safety plan should be in place to provide these patients with the support they need, such as providing phone numbers for or access to counsellors or psychologists.

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

1. Please make clear that the study treatment has only been tested in healthy adults.
2. Please insert the study schema as well as the following table on pages 12-14 of the study protocol into the Participant Information Sheet and Consent Forms.
3. Please include information on the procedures in the event of hospitalisation, included in the consent form, in the Participant Information Sheets.
4. Please amend the Participant Information Sheet and Consent Forms, moving the contact details at the end of the forms.
5. The Pregnant Partner Participant Information Sheet and Consent Form should be re-named the Pregnant Participant Information Sheet and Consent Form, and amended throughout to refer to the pregnant participant rather than the partner.
6. The Committee queried whether the participant was capable of full informed consent. The Researcher confirmed that the participant is capable. The Committee stated that if this is the case, consent of the parents is not needed and compensation for participation should go to the consenting participant. Please remove the Parent/Caregiver Participant Information Sheet and Consent Form, and amend the Participant Information Sheet and Consent Form to address a consenting child. Please also amend it to state that the participant will receive compensation.
7. Please proofread the Participant Information Sheet and Consent Form to address the specific participant, e.g. removing “and if male” under ‘Pregnancy’ (page 4).

Decision

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

1. Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* paragraph6.22).
2. Please create a safety plan in the case that any mental health concern is detected in assessing the questionnaire documents, and update the Participant Information Sheet and Consent Forms to include that (*Ethical Guidelines for Intervention Studies* paragraph6.62).

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| **5** | **Ethics ref:** | **18/CEN/267** |  |
|  | Title: | DCR PHXC-301 - Roll-Over Study to Evaluate the Long-Term Safety and Efficacy of DCR-PHXC in Patients with Primary Hyperoxaluria |  |
|  | Principal Investigator: | Dr William Wong |  |
|  | Sponsor: | Pharmaceutical Solutions Ltd |  |
|  | Clock Start Date: | 20 December 2018 |  |

Dr William Wong was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This is the extension-study following the previous application (18/CEN/266). This study was reviewed together with the previous study, and the ethical issues raised and requested changes to the Participant Information Sheet and Consent Forms are the same.

Decision

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

1. Please amend the information sheet and consent forms, taking into account the requests of the committee mentioned in the review of application 18/CEN/266 (*Ethical Guidelines for Intervention Studies* paragraph6.22).
2. Please create a safety plan in the case that any mental health concern is detected in assessing the questionnaire documents, and update the Participant Information Sheet and Consent Forms to include that (*Ethical Guidelines for Intervention Studies* paragraph6.62).

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| **6** | **Ethics ref:** | **18/CEN/263** |  |
|  | Title: | The COAST pilot initiative |  |
|  | Principal Investigator: | Dr Amanda Sommerfeldt |  |
|  | Sponsor: | Southern DHB |  |
|  | Clock Start Date: | 20 December 2018 |  |

Dr Yih Harng Chong and Dr Amanda Sommerfeldt 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 study wishes to implement and evaluate the COAST initiative. The COAST initiative aims to coordinate care for patients in their final year of life. The COAST form is intended to be a medical directive completed by a practitioner when treatment beyond the recorded ceiling of care is not clinically appropriate. The study will evaluate whether the COAST form is acceptable to patients, their families and to health practitioners, as well as its effectiveness. The COAST initiative has not been used in New Zealand before, but has been trialled in the US and Australia; the study will assess its suitability in a new setting.

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 it is not possible for HDECs to approve an application unless it is consistent with New Zealand Law. Heath or disability Research involving participants who are not competent to consent must be undertaken in accordance with Right 7(4) of the of the Code of Health and Disability Services Consumers’ Rights. Right 7(4) of the Code requires that any services provided without the informed consent of an incompetent consumer must be in the best interests of the consumer. This means that there must be some benefit, or potential benefit, to the participant beyond what they would receive if they were not participating in the research. In addition participation must be either consistent with the informed choice the person would have made if competent or the provider must take into account the views of other available suitable persons interested in the welfare of the person.
2. The Committee noted that proxy consent by a welfare guardian or EPOA is only legally acceptable if a “medical experiment” was intended to save the person’s life or prevent serious damage to the person’s health. However, this research does not appear to be a “medical experiment” so a welfare guardian or EPOA may be able to give consent on behalf of an incompetent person if participation was in the person’s best interests (PPPR Act).In that case the EPOA must have been invoked by medical certification and the EPOA’s or welfare guardian’s appointment must give these powers to the proxy.
3. Therefore the documents should only be used to gauge the views of relatives/ friends/ of potential participants who are unable to consent for themselves. This means that the forms should not involve language whereby the relative/friend consent on behalf of someone else. The language should reflect that the document seeks the friend/relative/EPOA’s view that the non-consenting person would be agreeable in participating or, if that is not known, seek those persons’ views.. This is in line with Right 7(4)cii: Once reasonable steps have been taken the provider can enrol an incompetent person provided enrolment is in their best interests.
4. The committee noted that it cannot give legal advice. If it is proposed to include incompetent participants the researchers should seek their own legal advice.
5. The Committee pointed out that although the Researcher had provided a form describing the Coast initiative, no document that gave the potential participant information about the study had been submitted, and as such the form was inappropriate as a Participant Information Sheet and Consent Form.

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

1. For a study of this kind to be accepted, the Committee stated that it would require separate Participant Information and Consent Forms for the patients, families and health practitioners, following 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:

* *Ethical Guidelines for Intervention Studies* paragraph6.26
* *Ethical Guidelines for Intervention Studies* paragraph6.22

The Committee recommended that legal advice be sought for this research before re-submission, to ensure that it is in compliance with New Zealand medical law. It suggested that the researcher also contact the Otago University Bioethics Research Centre for advice.

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| **7** | **Ethics ref:** | **18/CEN/268** |  |
|  | Title: | The SORE Study |  |
|  | Principal Investigator: | Dr Marinus Stowers |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 20 December 2018 |  |

Dr Marinus Stowers was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The study investigates the use of intraosseous ropivacaine in Anterior Cruciate Ligament (ACL) reconstruction. Due to the lack of literature on the safety profile regarding the safety of ropivacaine being used in the lower limb, the researcher is proposing a pilot study. Previous studies have looked at using local anaesthetic, but in the upper limb, so there is discrepancy regarding the amount and dose used to ensure pain reduction and safety. This is a safety trial, with 15 participants in total divided into three groups, two of which will receive two different doses of ropivacaine, and a control group which will receive the standard care. It aims to measure local anaesthetic levels using an arterial line into the wrist, which will also be used to monitor blood pressure. Patients undergoing ACL reconstruction will receive a tourniquet (a tight cuff around the upper thigh) to simulate a bloodless field. The surgery can last from 45-90 minutes. The tourniquet is intended hold the local anaesthetic within the limb. A needle will introduce the anaesthetic into the bone, anaesthetising the entire limb.

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 information on the study sponsor was not included in the application form, but is required.
2. The Committee stated that for future reference, in answering question p.4.1 it would be helpful to provide statistics regarding the prevalence of this disease in Maori.

Summary of outstanding ethical issues

1. The Committee queried whether Maori were being excluded from the study. The Researcher stated that they are not being excluded. The Committee expressed their concern regarding the researcher’s answer to question p.4.3, that Maori consultation is not required, and stated that in fact consultation is required if Maori are to be included in the study. The Researcher agreed to seek Maori consultation.
2. The Committee stated that a ‘rescue’ plan/protocol is required, so that, in the case that the participant is in extreme pain, there are provisions to reduce pain.

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

1. In the risks/benefits section, please add:  
   i. that the procedure of introducing ropivacaine using a needle will not last significantly longer than the standard of care.  
   ii. that a tourniquet will be used during the surgery, regardless of the potential participant’s involvement in the study  
   iii. that a result of the procedure could be that the participant will be able to mobilise earlier.
2. The Committee requested that the name on the heading of the Participant Information Sheet be changed so as not to discourage potential participants from participating in the study.
3. Please explain in the Participant Information Sheet that ropivacaine could be less effective than the standard of care.
4. Please include information on timeframes to the flow diagram.
5. Please explain what all acronyms in the Participant Information Sheet mean the first time they appear.
6. The Committee noted that the PIS reads optimistically that the procedure is going to work and be better, but that this is not yet known. It states that it can provide “good pain relief” and that the participant will “leave the operating room with minimal pain in the leg”. Please remove these statements.
7. Please convert to simple English all expressions that the average person may not understand, such as “and range from hematoma formation, temporary occlusion and local infection” (page 3).
8. The Committee asked for the reference to the “60-minute mark” at the bottom of page 3 to be clarified: 60 minutes since when?
9. Please add a Maori contact number.
10. Please amend the Participant Information Sheet specifying who will be performing each step in the research process.
11. On the PIS under ‘what are my rights”, please include the participant’s right to request correction of their personal health information.
12. Please add a telephone number under the section “who do I contact for more information if I have concerns” on pages 4/5.

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* paragraph6.22).
* Please provide evidence of Maori consultation (*Ethical Guidelines for Intervention Studies* paragraph4.9).
* Please create a safety plan in the case that the participant is in extreme pain, and update the protocol, as well as the Participant Information Sheet and Consent Forms to include that (*Ethical Guidelines for Intervention Studies* paragraph6.62).

This following information will be reviewed, and a final decision made on the application, by Mrs Leesa Russel and Dr Cordelia Thomas

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| **8** | **Ethics ref:** | **18/CEN/279** |  |
|  | Title: | (duplicate) Fatigue After STroke Educational Recovery trial (FASTER) |  |
|  | Principal Investigator: | Dr Kelly M. Jones |  |
|  | Sponsor: | Auckland University of Technology |  |
|  | Clock Start Date: | 10 January 2019 |  |

Dr Kelly Jones was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The study is a full-scale randomized control trial testing a new treatment for fatigue, which is a cognitive behavioural-based program. It aims to assess the effect of the intervention on reducing physical, psychological and mental fatigue and improving quality of life in stroke survivors against the alternative for standard of care.

Summary of resolved ethical issues

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

1. The Committee stated for future reference that an ethical issue in this study for Maori participants is that of whakama (shame).
2. For future reference, the Committee stated that acronyms that imply the success of a study should not be used.

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 preventing or restricting participants from receiving the results of the study is inappropriate.

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

1. Please ensure that it is consistently stated throughout the forms that the data collected will be stored for 10 years. Please also amend to correctly state who will be responsible for storing the data.
2. In the the Participant Information Sheet and Consent Form, under the heading “what will happen in this research”, the sentence “If they are willing, we will also be asking questions [of] the caregiver (family member or friend) who provides you with the most support” should be bolded.
3. The Committee expressed that the family/whanau section of the Participant Information Sheet and Consent Form is unclear. Please clarify at the start of this section that the purpose is to elicit the views of the family member about the care of their family member who has had a stroke.
4. Please have all Participant Information Sheet and Consent Forms proofread by a person outside of the research team.
5. The Committee requested that the following compensation wording be added to all Participant Information Sheet and Consent Forms: “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.”
6. In both Information Sheets, please specify exactly how vouchers will be given to participants and caregivers, noting that caregivers may be from a different family/whanau.
7. Please explain in the Information Sheets what the safety protocol(s) will involve, ensuring that this takes into consideration that several questions in the questionnaires could cause distress in some participants. A safety plan would need to ensure that participants can access the support they need, such as providing phone numbers for or access to counsellors or psychologists. Furthermore, note that depression and elder abuse are possibilities in post-stroke patients.
8. Please remove the yes/no tick boxes from the consent form for all statements that aren’t truly optional, that is a participant could select ‘no’ and still participate in the study.
9. Please reformat the contacts section on page 4 so that the Health and Disability Ethics Committee contact information is not under the heading “Cultural support”.

Decision

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

* Please amend the information sheets and consent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* paragraph6.22).
* Please update the study protocol, ensuring that participants will have access to the study results (*Ethical Guidelines for Intervention Studies* paragraph7.21).

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

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| **9** | **Ethics ref:** | **18/CEN/275** |  |
|  | Title: | A clinical study to test how effective and safe GLPG1690 is for participants with idiopathic pulmonary fibrosis (IPF) when used together with standard medical treatment |  |
|  | Principal Investigator: | Prof Lutz Beckert |  |
|  | Sponsor: | PPD |  |
|  | Clock Start Date: | 10 December 2018 |  |

Prof Lutz Beckert 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. Individuals with IPF have a survival rate of 2.4 to 3.2 years. Two treatments have recently become available, but they do not cure IPF, they only make it progress slower with a number of side-effects. The medication considered is to be used in addition to the two currently available treatments. If patients wish to participate, they will maintain their active treatment and will be randomised to the add-on tablets or placebo.

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 noted that several questions in the questionnaires could cause distress in some participants and strongly recommended that a safety plan would be in place to provide these participants with the support they need, such as providing phone numbers for or access to counsellors or psychologists.

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

1. On page 3 of the Information Sheet, it refers to the “Consent Form”. Please amend to “Information Sheet”.
2. On page 3, the Information Sheet refers to testing for hepatitis B and C, and HIV. Please add that those are notifiable diseases.
3. Please re-write the sentence “details of any relevant concomitant medicinal products” on page 3 of the Pregnant Partner Information Sheet and Consent Form” in lay language.
4. On the Pregnant Partner Consent Form, page 6, please expand or amend the section beginning with “I understand that this pregnant partner release of information sheet is linked to…” explaining what is meant by ‘linked’.
5. The Pregnant Partner Release of Information Consent Form, page 6, refers to “information about my health and my sex life”. Please explain exactly what type of information is requested about “sex life”, and ensure that this is outlined in the Information Sheet.
6. The Committee stated that a representative signing on behalf of adults is not legally possible in New Zealand. Please remove all references to a legal representative in the Pregnant Partner Release of Information Consent Form.
7. The Committee stated that participants are unable to consent on behalf of their children until those children are born alive. It requested that all sections in the Pregnant Partner Release of Information Consent Form consenting to a future child be removed, and included in a separate page to be signed once the baby is born.
8. On page 2 of the Optional Genetic Participant Information Sheet and Informed Consent Form section 4, please amend the 4th bullet point to specify whether it refers to IPF or to other diseases as well.
9. Please outline the safety plan in all Information Sheet and Consent Forms, with specific attention to the outcome of mental health issues being detected from the results of the questionnaires.
10. Please specify in each case where it is mentioned in the Information Sheet and Consent Forms that the researcher may contact the participant’s GP.

Decision

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

* Please amend the information sheets and consent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* paragraph6.22).
* Please create a safety plan in the case that any mental health concern is detected in assessing the questionnaire documents, and update the Participant Information Sheet and Consent Forms to include that (*Ethical Guidelines for Intervention Studies* paragraph6.62).

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

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| **10** | **Ethics ref:** | **18/CEN/276** |  |
|  | Title: | (duplicate) Study of VTS-270 (2-hydroxypropyl-β-cyclodextrin) to Treat Niemann-Pick Type C1 (NPC1) Disease |  |
|  | Principal Investigator: | Dr Kelly Byrne |  |
|  | Sponsor: | Pharmaceutical Solutions Ltd |  |
|  | Clock Start Date: | 10 January 2019 |  |

Dr Kelly Byrnee was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This is a phase 2b/3 clinical study which consists of 3 parts, Parts A, B and C. Only Part C will be conducted in NZ and only 1 patient will be recruited. This New Zealand-based patient completed Part B and is currently participating in Part C in Australia.

Part A has concluded and was conducted in the UK and USA and its objective is to determine the optimal dose of VTS-270, which will be used in Parts B and C. Dose selection criteria include safety and tolerability including a thorough audiological evaluation. 1 in 4 patients (25%) enrolled in Part A will not receive VTS-270 (control arm).

Part B will evaluate in a double-blind sham-controlled design the progression of the neurological manifestations of NPC1 disease after 52 weeks of treatment. The composite efficacy outcome consists of 4 components of the NPC Clinical Severity Scale: ambulation, fine motor skills, cognition and swallowing. 1 in 3 patients (33%) enrolled in Part B will not receive VTS-270 (control arm). All Part B patients have completed this portion of the study.

Part C will evaluated the long-term safety, tolerability and efficacy of the dose selected for Part B. All patients in this part will be from Part A and B and receive VTS-270.

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 the treatment was in the best interest of the single participant. Dr Kelly Byrne confirmed that after meeting with the patient’s primary care doctors and with the patient he is convinced that the treatment is in their best interest. Dr Kelly Byrne also expressed his belief that the patient was able to indicate some consent through gestures and other behaviours, and confirmed his understanding that he would stop treatment if the patient at any time appears to resist it.

Decision

This application was *approved* by consensus.

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| **11** | **Ethics ref:** | **19/CEN/4** |  |
|  | Title: | Medication use in breast cancer patients |  |
|  | Principal Investigator: | Dr Sandar Tin Tin |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 10 January 2019 |  |

No member of the research team 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

1. Cancer patients are commonly burdened with comorbidities and often use multiple medications. This may have an impact on cancer treatments and outcomes. This research aims to investigate the use of prescription medications for non-cancer related indications in women with primary invasive breast cancer. The data consolidated from four regional breast cancer registers will be used, which covers about 63% of all breast cancer registrations in New Zealand. Patient data will be linked to a number of health datasets held by the Ministry of Health. The findings will provide insight into medication use and related consequences in breast cancer patients in New Zealand, and will inform policy, practice and efforts to improve cancer care and outcomes and reduce inequities.

Summary of resolved ethical issues

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

1. The Committee stated that for future reference, in answering question p.4.1 it would be helpful to provide statistics regarding the prevalence of the disease in Maori.

Decision

This application was *approved* by consensus.

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| **12** | **Ethics ref:** | **18/CEN/282** |  |
|  | Title: | Test for Chlorine Exposure |  |
|  | Principal Investigator: | Dr Ross Boswell |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 10 January 2019 |  |

Dr Ross Boswell was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The study aims to assess a test for chlorine exposure. It is a human observational study: a population commonly exposed to low-level chlorine gas such as competitive swimmers, their coaches, and swimming pool attendants will be identified and invited to participate. A suitable control population, track athletes in training and their coaches, will be similarly invited. Those who agree will be asked to provide details of their recent exposure to chlorinated pools and chlorine products, and blood and urine specimens will be collected for analysis.

Since chlorotyrosine and nitrotyrosine are generated by the inflammatory response, it is proposed to use anonymised leftover blood and urine specimens from patients admitted to Middlemore Hospital with confirmed pneumonia as a second control population.

The specimens will undergo preliminary processing in the Middlemore Hospital Laboratory and then be sent to the OPCW (Organisation for the Prohibition of Chemical Weapons) Laboratory in the Netherlands for assay.

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 the researcher was going to approach pneumonia patients to ask for their consent, and whether that would happen before or after accessing their identifiable health information. The Researcher agreed that he would identify potentially useful samples without accessing any identifiable health information, and then have a clinician in the laboratory de-identify the samples so that the Researcher can subsequently analyse them. In doing so, no identifiable health information would be accessed during that part of the research and consent to access the leftover samples of the pneumonia patients would not need to be sought.
2. The Committee noted for future reference that cultural issues involved in this research for Maori include the fact that samples are being sent overseas, and that data is a Taonga (a treasure) that should be looked after.

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 independent peer review is required, and specifically by a reviewer outside of the research team. See *Ethical Guidelines for Observational Studies 2012* (appendix): Peer review delivers an objective opinion: Those acting in the capacity of reviewers are charged with delivering a balanced and considered analysis of the research. Generally, the success of the peer review process is determined by the extent to which these evaluations can be considered free of bias, equitable and fair. Objectivity can be compromised if peer reviewers have conflicts of interest, and so appropriate peer reviewers typically will not be materially connected to the researcher(s) in a way that might undermine objectivity, and be free from either positive or negative inducements.

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

1. The Committee stated that the reference to the Syrian conflict on the first page is emotive and puts pressure on the potential participant. Please remove all references to it.
2. Please make explicit and emphasise that there are no new blood tests involved for the participant in this study, but only the use of samples already taken.
3. Please remove the yes/no tick boxes from the consent form for all statements that aren’t truly optional, that is a participant could select ‘no’ and still participate in the study.
4. Please include Maori contact details.
5. The Committee queried the lack of a Māori tissue statement in the Participant Information Sheet. The Committee recommended the following statement: “You may hold beliefs about a sacred and shared value of any tissue samples removed. The cultural issues associated with sending your samples overseas and/or storing your tissue should be discussed with your family/whanau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult prior to participation in research where this occurs. However, it is acknowledged that individuals have the right to choose.”
6. Please detail precisely where the samples sent overseas will go, and what will happen to them afterwards.
7. Please remove the section “I consent to the research staff collecting and processing my information, including information about my health” from the Consent Form.

Decision

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

* Please amend the information sheet and consent forms for the pneumonia patients, taking into account the suggestions made by the committee *(Ethical Guidelines for Observational Studies* paragraph *6.10)*.
* Please submit information sheet and consent forms for both the swimmer and track-runner participants *(Ethical Guidelines for Observational Studies* paragraph *6.10)*.
* Please submit the surveys/questionnaires to be used in the study *(Ethical Guidelines for Observational Studies* paragraph *6.29)*.
* Please submit evidence of independent peer review (*Ethical Guidelines for Observational Studies 2012* appendix: Core features of the peer review process).

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

Due to the time pressure of the study, the Committee stated that the Researchers could prepare the PIS forms and send them in before the official HDEC letter is sent.

## 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 February 2019 |
| **Meeting venue:** | Room GN.6, Ground Floor, Ministry of Health, 133 Molesworth Street, Wellington |

The meeting closed at 4:30pm.