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| **Committee:** | Central Health and Disability Ethics Committee |
| **Meeting date:** | 24 July 2018 |
| **Meeting venue:** | Room GC.1, 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 26 June 2018 |
| 12:30pm | New applications (see over for details) |
|  | i 18/CEN/125  ii 18/CEN/126  iii 18/CEN/127  iv 18/CEN/129  v 18/CEN/130  vi 18/CEN/131  vii 18/CEN/132  viii 18/CEN/133  ix 18/CEN/134  x 18/CEN/137 |
| 4:45pm | General business:   * Noting section of agenda |
| 5:00pm | 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 |
| Mrs Sandy Gill | Lay (consumer/community perspectives) | 30/07/2015 | 30/07/2018 | Present |
| Dr Patries Herst | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | Present |
| Dr Dean Quinn | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | Present |
| Dr Cordelia Thomas | Lay (the law) | 20/05/2017 | 20/05/2020 | Present |
| Dr Peter Gallagher | Non-lay (health/disability service provision) | 30/07/2015 | 30/07/2018 | Present |

## Welcome

The Chair opened the meeting at 12:05pm and welcomed Committee members.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

## Confirmation of previous minutes

The minutes of the meeting of 26 June 2018 were confirmed. It was noted that the 18/CEN/103 comments didn’t line up with the changes approved and was agreed that the Chair be sent a final copy of the minutes following tracked changes being made for approval by the Chair.

## New applications

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| **1** | **Ethics ref:** | **18/CEN/125** |
|  | Title: | Peritonsillar abscess: the microbiome |
|  | Principal Investigator: | Dr James Johnston |
|  | Sponsor: | University of Auckland |
|  | Clock Start Date: | 12 July 2018 |

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 the study

1. The Committee’s noted it’s understanding that in this study the researchers plan to take three swabs from patients who present at hospital with Peritonsillar Abscess (PTA) and who are having the PTA drained. The researchers plan to do RNAseq on 16SRNA to see: 1: what types of bacteria are found in the abscess and 2: whether there is a difference between the types of bacteria in the abscess, the tonsil and further down the throat.

Summary of outstanding ethical issues

1. The Committee queried why the researchers are not planning to take salvia as a fourth swab for testing. The researchers are looking to see where the bacteria might come from and it may be that it comes from the general population of bacteria present in the mouth. The Committee noted that a fourth swab with saliva to test whether bacteria are ubiquitous or specific to the tonsil could help to answer the study question.
2. The Committee queried whether 20 participants would allow for study results to be adequately powered and also what the known statistics for this study are based on if the microbiome of PTAs is not known.
3. The Committee queried how well the patient epithelial cells would survive at minus 20 degrees Celsius amongst all the bacteria and in relation to this queried why the researchers have stated that they intend to give participants the option to get their samples back. There are likely to be some MRSA positive staphs and streps in those samples and the Committee questioned the safety of sending the samples back.

The Committee requested the following changes be made to the participant information sheet and consent forms.

1. The Committee noted that the NEAC guidelines set out the standards that need to be met in the interests of potential participants making a fully informed decision about whether or not to take part in a study. While the planned study is a relatively straight forward study the Committee agreed that the participant information sheet and consent form would need a substantial rewrite to bring it in line with the requirements of the guidelines. In with this in mind and weighing against the operational requirements the Committee agreed that it would be best to decline this study to allow the research team to rewrite the information sheet and consent form taking into account the following points and to resubmit the application for review.
2. The Committee noted its general observation that the participants will likely not have a lot of time to consider the information in the participant information sheet as they will be in the waiting room for their abscess to be drained when they are presented with the information and asked to consider being in the study. For ease of reading from a reader perspective the committee asked that the researchers revisit the document and reformat using single line space and less white space and that the pages be numbered.
3. The Committee noted that the information sheet is light on information and that they also refer to the template provided on the HDEC website: <https://ethics.health.govt.nz/guides-templates-forms-0/participant-information-sheet-templates> as a guide for what to include. At the same time the Committee asked that the researchers review the document for repetition of information and to be clearer about the purpose of the study and what will be required of participants.
4. Page 1, paragraph 1, sentence 1: “to see what bacteria are in the abscess you have in your mouth” could better read as “what types of bacteria” are in the abscess you have in your mouth.
5. Page 2 under the heading ‘What is the purpose of this study?’: Please include a statement that informs the participants that the human body contains its own microflora, with many beneficial bacteria found on the skin, in the gut and inside the mouth. Note that some bacteria can be harmful when they form an abscess in the mouth and state that the identity of the types of bacteria that are found in the abscess is not known and that is why you are doing this study.
6. Page 2: please note that the “ethical aspects” of this study have been approved by the Central Health and Disability Ethics Committee.
7. Pages 2 and 3: please also include Prof Richard Douglas’ contact details on the last page of the document under the heading ‘Who can I contact for more information or if I have concerns?’
8. Page 4 under the heading ‘What are the possible benefits and risks of this study?’: the Committee queried what the possible future benefits of this study might be such as “better devices and medications”. If the researchers are referring to possible known treatments or devices for example, antibiotics then please state this. Alternatively they could state something along the lines of this will allow us to increase our knowledge about how PTAs form and are best managed/treated.
9. Page 4 under the heading ‘what if something goes wrong?’: please update the compensation statement with the following:

*If you were injured in this study, 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.*

1. Page 5 under the heading ‘What happens after the study or if I change my mind?’: The Committee noted the statement “Where such use [of the raw data] goes beyond that outlined in the present application, further ethical approval will be sought” and asked that the researchers clarify what is meant by this and whether it includes future unspecified research on the samples. If future unspecified research is planned on the samples the research team will need to submit a separate information sheet and consent form that specifically asks for consent to retain the samples for future unrelated analysis. Please also describe how participants’ data will be anonymised, for example by using trial specific numbers and not their names, date of birth on the swabs taken. Please also include more detail about who has access to participants’ health data, for instance HDEC or regulatory authorities as part of an audit.

Decision

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

* *Free and informed consent, paras 6.10 and 6.11 of the NEAC Guidelines for Observational Studies*

The Committee noted that the NEAC guidelines set out the standards that need to be met in the interests of potential participants making a fully informed decision about whether or not to take part in a study. While the planned study is a relatively straight forward study the Committee agreed that the participant information sheet and consent form would need a substantial rewrite to bring it in line with the requirements of the guidelines. In with this in mind and weighing against the operational requirements the Committee agreed that it would be best to decline this study to allow the research team to rewrite the information sheet and consent form taking into account the points raised and to resubmit the application for review.

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| **2** | **Ethics ref:** | **18/CEN/126** |
|  | Title: | Promis 1\_A clinical study of inhaled CMS by i-Neb in patients with NCFB |
|  | Principal Investigator: | Dr Paul Dawkins |
|  | Sponsor: |  |
|  | Clock Start Date: | 12 July 2018 |

Mrs Catherine Howie, Dr William Good and Dr Conroy 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 the study

1. This study is planned for patients who have non-Cystic Fibrosis bronchiectasis who are colonised with a particular bacterium called *Pseudomonas aeruginosa* that is causing inflammatory infective flare-ups leading to progressive tissue damage. Participants will need to have had at least two flare-ups to be eligible to enter the study. Participants will know that they have the condition and will have been getting infections on regular basis. This study will trial a new drug that could cut down the number of flare-ups and cut down on doctor visits by killing the bacteria in the lungs. Other similar drug trials have been successful but have not met the reduction in flare-ups. The trial drug is a known and safe drug, has been designed to be nebulised and is licenced in the UK and Australia.
2. Participants will be asked to be in this study for 12 months and the recruitment window is 18 months. The pool of potential participants will be across several sites with the aim to recruit 5-10 people from New Zealand.

Summary of resolved ethical issues

1. Form for Withdrawal of Participation: The Committee noted that people can withdraw from the study without having to sign a form. The researchers acknowledged this and confirmed that this form is not compulsory for patient noting that the study investigator can document a participant’s withdrawal. On the form itself there is a box that provides for the investigator to document this if the decision to withdraw is communicated verbally.
2. The Committee queried who will make the initial approach to participants to invite them to be in the study. Question r.5.4 on page 23 of the application form indicates that the potential participants are already in a patient relationship with the study doctor and the Committee noted that if that is the case the initial approach will be best made by a third party independent of the study. The researchers clarified that once a potential participant is identified by the consultant that person informs the research nurse who then makes contact with the patient. While the initial contact is with the consultant the next step is done by the research nurse so there is independence and time given to people to consider whether they will participate or not.
3. In relation to the cultural questions in the application form the Committee noted that it was good to see statistics and information provided there and noted, for future reference, that it is helpful for any known statistics in relation Pasifika and other non-Maori ethnic minority communities to be stated at question f.1.2.on page 28 of the application form.
4. The Committee queried whether or not there will be any instruction given to participants on taking usual medications in relation to the study drug. The researchers advised that most medications can be continued. Will there be the usual maintenance in terms of timing to take usual medications prior to the dosing of this study drug? The Researchers advised that they will have to look into that and come back to the Committee with an answer. The Committee noted that it would be useful to have this information, once known, in the information sheet as many of the study participants will be on other medications so it will be useful to give uniform advice on when taken in relation to study medication.

The Committee requested the following changes be made to the participant information sheet and consent forms.

1. The Committee noted its observation that there is a tension between being succinct with complex information and congratulated the researchers on including a grid in the participant information sheet noting it is helpful for potential participants.
2. Please head the information sheet and consent forms up with a layperson title.
3. The Committee noted that some participants will be in the placebo group for the duration of the trial (12 months) and asked what treatment participants in this group will receive if they have exacerbation. The researchers confirmed that they will continue on standard of care treatment and including intravenous antibiotics in the event they experience more severe episodes. Please include a sentence in the information sheet that advises participants that should they be in the placebo group that they will still have access to standard of care treatment.
4. The Committee noted that participants are advised that they can request a summary of results at the end of the study and asked that instead the researchers offer this to them at the end of the study. Given the duration of the study is 12 months participants may forget about the possibility.
5. Page 2: please remove the word “germs” and replace it with the word “bacteria”.
6. The Committee noted that page 13 of the participant information sheet submitted notes that “site to include their text related to the use of tissue samples” and suggested that the researchers use the cultural statement from the HDEC template here. The researchers explained that they have a request from their Tainui consultant to include a statement here. The Committee asked that that statement be provided.
7. Page 16 under the heading ‘Complaints and compensation’: Please revise the statement provided here as it implies that compensation would automatically be provided when this is not the case. You may wish to include the following statement:

*If you were injured in this study, 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.*

1. The Committee queried if there will be any instruction given to participants on taking usual medications in relation to the study drug. The researchers advised that most medications can be continued. Were there any guidelines on the timing of participants taking their usual medications, i.e. prior to or after the dosing of this study drug? The Researchers advised that they will have to look into that and come back to the Committee with an answer. The Committee noted that it would be useful to have this information, once known, in the information sheet as many of the study participants will be on other medications so it will be useful to give uniform advice on when taken in relation to study medication.
2. Consent form – Please revisit and only include Yes/No options for statements that are truly optional. For example, statement 4.
3. Please include provision for participants to consent to their samples being sent overseas.
4. Optional PIS for FUR Page 1 under the heading ‘Introduction’: please correct the typo “resistance” with “resistant”
5. Pregnancy follow-up form Page 2, paras 2-3: the Committee noted switching between reference to “unborn baby” and “baby’s health”. It is currently unclear whether the Researchers mean they are requesting information after the birth or whether they are looking at the pregnancy and the Committee noted the need to be clear about which one the Researchers are talking about. If they want to follow up after baby is born the Committee reminded the Researchers that the mother can’t give consent until after baby is born.

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*).

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

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| **3** | **Ethics ref:** | **18/CEN/127** |
|  | Title: | Bactek-O Sublingual Vaccine Treatment in Bronchiectasis - A Pilot Study |
|  | Principal Investigator: | Dr William Good |
|  | Sponsor: | The University of Auckland |
|  | Clock Start Date: | 12 July 2018 |

Dr William Good and Mrs Catherine Howie 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 resolved ethical issues

1. The Committee congratulated the Researcher on the submission of a well completed application.
2. The Committee sought clarification of the status of the study medicine in New Zealand. It is currently not licenced, the Researchers have applied to SCOTT and a decision is currently pending.
3. The Committee noted the potential conflict of interest for the lead researcher as treating physician and as someone who may make the initial approach to potential participants. The Researchers explained that patients will be identified by the treating consultant and then that a Research Nurse will make the approach about participation in the study; they will be given the information sheet and will have time to consider the information before deciding whether or not to take part. There will be emphasis placed on participation being voluntary and that non-participation will not affect day to day treatment. The Committee was satisfied that participation will be voluntary and that patients will be given sufficient time and education around what is involved.
4. The Committee congratulated the Researchers on the answers given to the cultural questions in the application form and noted in particular the answer stated at question f.1.2 that included statistics for Pacific Island and non-Maori populations.

Summary of outstanding ethical issues

1. The Researcher noted that an amendment has been made to Page 14 of the study protocol after submission of this application. At the second to last bullet point “9 months” has been deleted. The Committee advised the Researcher to submit this as a protocol amendment following approval of this study.

The Committee requested the following changes be made to the participant information sheet and consent forms.

1. Please review the document and replace the word “subject” with the word “participant”.
2. The Committee noted that it had trouble understanding the randomisation process and relative chance of receiving treatment as it is currently not explicitly stated whether participants have a 50/50 chance. Please make this clearer in the information sheet.
3. The Committee noted that exclusion and inclusion criteria are listed and that a couple could be interpreted incorrectly such as “taking continuous oral steroids or other immune supressing medications for more than 6 weeks”. The Committee asked whether this includes current use. The Researchers advised that the timing would include having recently been on them. The Committee asked that the Researchers make exclusion criteria clearer.
4. The Committee asked that the Researchers be more forthcoming with the information about the experience of hypertonic saline and that the potential side-effects be made more explicit.
5. Page 1 under the heading ‘Introduction’: please included the words “ethical aspects” have been approved by the Central Health and Disability Ethics Committee.
6. The Committee noted that the Consent form makes reference to participants’ GPs being informed of their participation in the study and asked that this be explained to participants in the information sheet first. The Researchers will encourage participants to let their GP know that they are part of this study so their GP will be aware in the event of any adverse events. If this is a requirement of participation the Researchers could speak to it in the information sheet as inclusion criteria.
7. Page 1 under the heading ‘Purpose of this study’: the Committee noted the statement that the main aim of this study is to assess whether Bactek-O can reduce inflammation in the lungs and asked that the Researchers state in this section what Bactek-O is.
8. Page 2 under the heading ‘Why have I been asked to take part?’ Please state here what the inclusion and exclusion criteria are directly underneath that and not on the next page.
9. Page 6 under the heading ‘Costs, Reimbursements and Payments’: The Committee noted the statement that travelling costs will be subsidized with a petrol voucher and asked the Researchers to phrase this more inclusively so that people who use public transport will also be reimbursed. Payment would be expected to be equal for all in the interests of fairness.

Decision

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

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| **4** | **Ethics ref:** | **18/CEN/129** |
|  | Title: | NORTH |
|  | Principal Investigator: | Dr Mark Winstanley |
|  | Sponsor: | Australia and New Zealand Children's Haematology/O |
|  | Clock Start Date: | 12 July 2018 |

Dr Mark Winstanley and Mrs 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.

The Committee requested the following changes be made to the participant information sheets and assent/consent forms.

1. The Committee queried whether this is a dose escalation study. The Researchers explained that the first patient will receive dosing as per the recommended dose and pharmacokinetic analysis will be done on that and then if that dose is shown to be okay then this will be used. It is not planned to escalate the dose beyond that. The Committee asked that this be made clear in the participant information sheet. The Researchers explained that the ideal is to have a dose bioactive at low level that is not toxic. This study is targeting how to get low level inhibition without the toxicity. Biological response together with Pharmacokinetic data showing what levels were achieved with response to treatment plan. It was suggested that the Researchers could state something along the lines of this study is being done to “help us find out whether a low continuous dose of Panobinostat will give a good response with acceptably low toxicity”.
2. The Committee noted the participant information sheets and assent forms submitted with this application are “for older children” and “for younger children” and noted that it prefers that these forms are age appropriate and state an age range such as 7-11 year olds and 12-15 year olds. The Researchers advised that they had made this change to older and younger children after discussion following previous reviews.
3. Younger children form: the Researchers noted that historically 7 years of age has been the lower limit for this age group and that the lower limit will be patient dependent. The Committee noted that a 7 year old child may have trouble understanding the content in the form as it is currently presented. It was noted that having information forms available for younger children that are picture based would help them understand what is involved and the Committee noted that in the past it has seen 7-10 year old assent forms from Starship that were superb. The Researchers reiterated that they were guided by feedback from previous studies that pictures should not be used and, that they will check on the specifics of this with the person who co-ordinates their studies and report back to the Committee.
4. The Committee noted that in 7 year olds should have informed assent and that it did not think that the current form was age appropriate. So even if pictures would not be used, the wording would need to be adjusted.
5. In the information sheets and assent forms for older and younger children, the Committee noted that information on page 2 that states participants need to stay in the study currently offers negative reasons, suggests no hope of the child going into remission and queried whether there is a possibility that they would stay in the study ‘until your condition improves’? The Researchers noted that they could include here until the 12 month completion of treatment – “until you have completed 12 months of study therapy”.
6. The Committee noted that the participant information sheets give precautions to take around the handling of this study’s hazardous medicine but that these don’t mention protecting other family members and children from it? The Committee asked that the Researchers think about what to inform people in relation to this and to explain in the information sheets what they need to do.
7. Consent form for parent/guardian: please state that the test samples will be sent overseas.

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*).

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

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| **5** | **Ethics ref:** | **18/CEN/130** |
|  | Title: | A study of the safety, efficacy and tolerability of Nexvax2 in patients with Celiac Disease |
|  | Principal Investigator: | Prof Richard Gearry |
|  | Sponsor: | ImmusanT, Inc. |
|  | Clock Start Date: | 12 July 2018 |

Jen Coetzee and Kerin Thompson 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.

Dr Dean Quinn declared a potential conflict of interest, and the Committee decided that he could stay in the room but would not be involved in the discussion or decision-making for this application.

Summary of resolved ethical issues

1. The Committee queried how people involved in the trial study will be involved in the endoscopy sub-study. The Researchers explained that participants who have one copy of the HLA gene identified as part of screening in the initial study will be offered participation in the sub-study.
2. For future reference the Committee noted that it would have been more helpful to state, at question p.4.1 on page 25 of the application form, any known statistics or information about Maori. The statement that “The study is open to participants from all ethnic groups who meet the study eligibility criteria” does not answer the question of how the study may or may not benefit Maori. Similarly, at question f.2.1 it would be helpful to state any known stats or information on other New Zealand populations including Pacific Island peoples and non-Maori New Zealanders.

Summary of outstanding ethical issues

1. The Committee noted its obligation to check that compensation insurance is equivalent to that that would be provided by successful ACC claims and asked the Researchers to ensure that they have checked that insurers are covering to ACC equivalent standards.

The Committee requested the following changes be made to the participant information sheet and consent forms:

1. The Committee noted that finding the balance between succinct and relaying complicated information in these forms poses a difficult tension.
2. The Committee noted that the font and spacing in the documentation is dense and this could make it hard to for the reader to maintain interest. That said, the Committee noted that the grid is also very helpful. The Committee noted that the Endo sub-study information sheet was a lot easier to read and the font and spacing was better.
3. The Committee queried whether the research team also talks each person through the information sheets. The Researchers confirmed that they do.
4. Pregnancy follow-up information sheet The Researchers confirmed their recollection is that this form is for the collection of data beyond the birth of the child. The Committee reminded the Researchers that if this is the case then they need to make sure that consent for the child is signed after the birth of the child as the mother cannot legally give consent on behalf of the child until the child is born.

Main PIS/CF .

1. Page 10, 4th paragraph. Please included the names of the countries that the samples will be sent to and when they will be discarded.
2. Page 14 under the heading ‘Females who are not of child-bearing potential’ states that if you are unable to have children then you should discuss your contraceptive options with the study doctor. The Committee queried why this statement is included in the case that someone is infertile. The Researchers explained that it is more a case of clarifying the situation with doctor as from a safety perspective the doctor would need to know why there is not a need to take contraception. The Committee noted that it would be kinder to express it in that way as if this is the case for someone then the way in which it is currently written could be distressing.
3. Page 16, 1st paragraph: The Researchers confirmed that compensation for time and travel expenses is under discussion and asked for feedback from the Committee in relation to this. Three out of three sites are covering travel and two out of three sites are covering additional stipend in terms of inconvenience as the third site has policy against this. The Committee noted that as long as people know at each site then that is okay to have a different policy but at the same time it would need to know how much the stipend being offered is to determine whether it would be considered to be an inducement.
4. Optional Endoscopy Sub-Study, please include the cultural statement about what will happen to test samples from page 10 of the main study. Please include in the consent form the samples will be sent overseas.

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 confirm that the study insurers are covering to ACC equivalent standards. (*Ethical Guidelines for Intervention Studies* *paras 8.4 and 8.5*).

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

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| **6** | **Ethics ref:** | **18/CEN/131** |
|  | Title: | OZM-063: Avastin treatment for low grade brain tumour |
|  | Principal Investigator: | Dr Stephen Laughton |
|  | Sponsor: | Australia and New Zealand Children's Haematology/O |
|  | Clock Start Date: | 12 July 2018 |

Dr Stephen Laughton and Ms Leani Fourie 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 resolved ethical issues

1. The Committee commended the Researchers on submitting a well-completed application and on the merit of the study noting it had few concerns in relation to this study.
2. The Committee congratulated the Researchers on the answer provided at question p.4.2 in the application form noting that is was “spot on”. In relation to question p.4.1 on page 26 of the application form the Committee noted that the answer stated at question f.1.2 belongs here as question f.1.2 covers ethnicities such as Pacific Island peoples, Asian and other non-Maori populations.

The Committee requested the following changes be made to the participant information sheets and consent/assent forms.

1. The Committee noted that it prefers that the forms are age appropriate. The Committee noted that 7 year olds should be able to give informed assent and that it did not think that the current form was age appropriate. The Committee asked that the Researchers review and rewrite in language that is age appropriate and that pictures be included if at all possible. The Committee noted that it has seen a number of great examples from Starship in the past that included pictures including in studies where the children receive a study drug and are randomised to different arms of the study. The Researchers noted that they were guided by feedback from previous studies that pictures should not be used and, that they will check on the specifics of this with the person who co-ordinates their studies and report back to the Committee.
2. If the samples are going overseas (to Toronto), please state this both in the information sheet and consent/assent forms.
3. Please include the following statement in relation to compensation in the older children assent form as they are old enough to understand this.

*If you were injured as a result of treatment given as part of this study, which is unlikely, you won’t be eligible for compensation from ACC. However, compensation would be available from the study’s sponsor, ImmusanT, Inc, in line with industry guidelines. We can give you a copy of these guidelines if you wish. You would be able to take action through the courts if you disagreed with the amount of compensation provided.*

*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.*

1. Please include third party contact details on all forms. In relation to this contact names and details should be at end of form and not halfway through so that people can access them easily
2. Continued participation upon reaching the age of consent form Page 1: please remove reference to legal contracts in the opening paragraph as this is not legally correct.

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 information will be reviewed, and a final decision made on the application, by Dr Patries Herst and Mrs Sandy Gill.

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| **7** | **Ethics ref:** | **18/CEN/132** |
|  | Title: | rEECur |
|  | Principal Investigator: | Dr Mark Winstanley |
|  | Sponsor: | ANZCHOG |
|  | Clock Start Date: | 12 July 2018 |

Dr Mark Winstanley 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.

The Committee requested the following changes be made to the Participant Information Sheets and Consent forms.

Main PIS

1. Page 9 under the heading ‘Will my taking part in this trial be kept confidential?’ The Committee noted that because information will be securely stored at the Cancer Research UK Clinical Trials Unit at the University of Birmingham that New Zealand privacy law will not apply as stated. Please remove this statement.
2. The Committee noted that it was indicated in the application that all scans will be fully identifiable and sent to other participating researchers. The Committee noted that the usual practice is that de-identified information is sent to other researchers and offshore. The Researchers are partnering with a number of different groups this may be a requirement to have all of that information and access to scans as well. The Committee requested that this be specified in the information sheet.
3. The researchers commented that their last trial followed the same protocol and that this may be a European specific study requirement. Most studies following GCP do not send identifiable data to third parties. ANZCHOG studies also do not require this. Normally NHI numbers are used to check match and samples/information is sent with an anonymous study number. Having only one number to check patient identity against may result in false identity. Sending identifiable information would circumvent such mistakes.
4. The Committee queried whether it thought this approach is acceptable given risk of identifiable data privacy breaches around the world. A lot of studies where treatment medications are changed, samples are sent with name of patient rather than number as treatment may be modified on that basis. The Committee suggested this should be stated up front for participants along with the risks.
5. Page 4, 3rd paragraph: please reword the statement that says “The study will investigate whether PET-CT is better than routine widespread disease is before and after treatment” as it is unclear as to what this means.
6. Page 9, 7th paragraph: Please describe the data as “de-identified” rather than linked-anonymised as if it is linked then it is not anonymised.
7. Main Consent form: Page 14, please delete the last statement in the last 2 consent statements as this refers to future unspecified research and should be consented for separately and as part of the consent form for Future Unspecified Research. Please remove reference to consent for remaining samples to be stored and used for future ethically approved research as this aspect of consent should be covered separately and as part of the FUR consent form.
8. The Committee asked that Researchers provide an age appropriate assent form for the “younger child” participants. The Researchers noted that previous Committees had asked that the age range be removed and that they will include more information in relation to this in the response to the Committee.
9. The Committee noted the peer review document from Health Hunter New England Local Health District noted a “clinical trials sub-committee” had reviewed the study protocol and asked how that committee was comprised. The Committee noted that it is mandated to check that independent peer review is done by people with expertise too to comment on a study protocol. The researchers will access the document and will provide this information in a response to the committee.

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 Dean Quinn and Mrs Helen Walker.

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| **8** | **Ethics ref:** | **18/CEN/133** |
|  | Title: | Safety and efficacy of switching to TAF from TDF and/or OAVs in Hep B subjects with renal and/or hepatic impairment |
|  | Principal Investigator: | Prof Edward Gane |
|  | Sponsor: | Gilead Sciences Pty Limited |
|  | Clock Start Date: | 12 July 2018 |

Prof Gane and Mrs Margaret Joppa 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 resolved ethical issues

1. The Committee thanked the Researchers for answering the cultural questions with statistics, information and sensitivity and commended them on the answers stated in the application form.
2. The Committee noted the information sheet contains question marks in relation to reimbursement to participants and asked the researchers whether the value amount stated in the application form will be added to the information sheet. The Researchers explained that participants will be reimbursed for transport costs and for those who complete the intensive PK study a one off payment will be given for their time as this is a 24 hour intensive PK study.
3. The Committee noted that there is a tension between providing comprehensive information in the information sheets and being succinct. In this regard the Committee noted that the grid is helpful and as is the summary of tests included in the information sheets.

The Committee requested the following changes be made to the participant information sheet and consent forms.

1. Main consent form The Committee noted that the form talks about storing samples for up to 15 years and that the FUR information sheet also states up to 15 years and queried how these samples differ. The FUR includes samples taken as part of the main study cannot be used if participants don’t sign the FUR consent. The Researchers stated that the FUR consent includes an elective sample and then those that are left over and that they would confirm this and let the Committee know. The Committee queried whether the left over samples would be destroyed if participants don’t consent to FUR. Occasionally sponsors retain samples without specifying and the Committee asked that the Researchers check that with the sponsor.
2. Page 3 list of bullet points in regard to the requirement for follow-up visits: Please clearly state that people who are cured will continue on safety follow up visits.
3. Page 16 under the title ‘What are your treatment options?’ The second statement is ambiguously. Please state that this is in relation to chronic Hep B with liver failure.
4. Page 18, 4th paragraph under the heading ‘What will happen to my test samples?’ infers that Hepatitis is a notifiable disease and HIV is not. Please change this to state “If your Hepatitis or HIV test results are positive […]”.Should say Hep or HIV is positive.
5. Please include third party contact details on the last page for accessibility.
6. Partner Pregnancy Follow up Consent Form. The Committee noted that it is unclear whether participants are being asked to consent for data about their pregnancy or for health information about their pregnancy after the baby is born noting that the term “Outcome of pregnancy” is an ambiguous one. A separate consent section for after baby is born doesn’t state what participants are consenting to. The Committee asked that it be made clearer as to whether consent is for information about development of the baby or about health or progress of the baby. The Researchers added that this is a theoretical issue as people on dialysis are infertile.
7. PK sub-study. Please include a statement for consent to samples being sent overseas.

Decision

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

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| **9** | **Ethics ref:** | **18/CEN/134** |
|  | Title: | ARISE FLUIDS Observational Study |
|  | Principal Investigator: | A/Prof Peter Jones |
|  | Sponsor: |  |
|  | Clock Start Date: | 12 July 2018 |

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 resolved ethical issues

1. The Committee had no ethical concerns in relation to this study where the Researchers intend to access clinical records of data that is routinely collected for statistical purposes.
2. The Committee agreed that no health services are being provided in this study and that the Code of Rights therefore does not apply in this case.
3. The Researchers plan to collect data from people’s records retrospectively, de-identify it and work out which dose is better. The Committee discussed whether it would ask the researcher to justify why they can’t ask for consent retrospectively but agreed that this was not necessary as it does fall within the exception so long as what they are doing is ethical. Further, the study is low risk and is a worthwhile study.
4. A Letter submitted with the application states the data belongs the property of the emergency department and the Committee would like to remind the Researchers that records belong to the patient.

Decision

This application was *approved* by consensus.

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| **10** | **Ethics ref:** | **18/CEN/137** |
|  | Title: | CONNECT-FX |
|  | Principal Investigator: | Dr. Andrew Marshall |
|  | Sponsor: |  |
|  | Clock Start Date: | 12 July 2018 |

Mrs Marina Dzhelali and Dr Andrew Marshall 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 resolved ethical issues

1. The Committee queried whether it is planned that parents/guardians will consent for participants who are aged 18 and younger? The Researchers confirmed that this is planned as all participants have the condition Fragile X and are intellectually disabled.
2. The Committee noted that in New Zealand parents/legal guardians can consent on behalf of a child/young person who is16 years old or younger but the Patient Code of Rights doesn’t anticipate global consent and the Researchers will need to do individual assessments to deem whether the child is competent to assess. The Committee noted that parents/guardians can give consent for children aged 18 and younger if they are deemed to be not competent to give consent (Care of Children Act provides for this).but the Researchers do need to show that competence has been assessed. If they are assessed as competent then the researchers will need to re consent them to the study and if not then parents can give consent for the child up to when they are 18 years old.
3. The Researcher clarified that they do not plan to enrol children over the age of 16 into this study. The children who may turn 16 while they are in this study should be offered the chance to re-consent to being in the study if they are assessed as competent.
4. The Committee noted the answer given at question p.4.1 on page 23 of the application form that asks Researchers to describe whether and how their study might benefit Maori and asked whether there are any known statistics relating to Fragile X syndrome in Maori. The Researchers noted that one of the challenges with the disability register is that outpatient events are not coded and there is currently no accurate way of capturing how many have Fragile X Syndrome. The Committee noted for future reference that this information would be helpful information to include at question p.4.1. The Committee also noted for future reference that the cultural issue of ‘Whakama’ could be included at question p.4.2. Whakama often gets overlooked and encompasses feelings of shame, embarrassment and a reluctance to talk about what is happening.
5. The Committee noted in a similar application to this recently reviewed that a withdrawal/tapering off of the study drug was included and asked whether in this study the participants need to have a tapering period. The Researchers explained that the plan is for the extension study to be offered to families afterwards and for those who participate in the extension study that a taper will happen as part of that study.

Summary of outstanding ethical issues

1. Please revisit insurance and guarantee for the Committee that this can be provided. The Researchers will upload the new certificate with any response to the Committee.

The Committee requested the following changes be made to the participant information sheets and consent/assent forms.

Child participation information sheets and assent forms

1. The Committee noted that the language in the information sheets and assent forms for the participants could be further simplified and pictorial aids included. The Researchers could then use their own experience and expertise in conjunction with the documents when talking about the study with the children. Please review the younger child (7-11) and the older child (12-15) forms and make as simple as necessary and the Researchers can then determine which is more appropriate for each individual child. The Committee noted that ‘Easy Read’ uses a combination of words and pictures and has been shown to work well for children with intellectual disabilities.

Assent form 7-11: Please review the document for Americanisms such as “mom” and “bug bite” and replace with the New Zealand equivalent.

1. The Committee noted that the information around the physical assessment for puberty in both forms includes the statement that participants may or may not want their parents to be there when the assessment is done and suggested that this be rephrased as “please let us know” whether they want parents to be there. The Committee also noted the statement that “people have had changes in their mood” and suggested that this be changed to read something along the lines of “people who have had this drug have had changes to how they feel”.

Assent form 12-15: please include contact details for people independent of the study who the participants can contact if they have any questions or concerns.

1. Please include the clause in relation to compensation from page 13 of the main PIS as some participants will have capacity to understand this.
2. Please remove the information that tells participants to be careful when driving as this age group is not likely to be driving.

Main participant information sheet and consent form

1. Pages 2-9: The Committee asked the Researchers to review the information on the different procedures as the information currently stated is repetitive in parts. The Committee commended the use of the table on page 4 on the information sheet but suggested that the Researchers consider grouping visits 2,3 and 5 together and visits 4 and 6 together as they appear to be similar. The Committee noted that in the interests of making the information accessible and understandable that it makes sense to summarise and state more clearly for participants.
2. Page 2 The Committee asked that the Researchers include information, after the statement that there are currently no medicines indicated to treat FXS; that this study drug has been trialled in open label studies but is not currently in regular use. Please also include information about what was found in the open label study as this will be useful information for the parent to know.
3. Page 8 under the heading ‘Application of the study drug at home’. The information about showering at home is the same information as on page 3 of the document and the Committee recommended removing this as it is repetitive.
4. Page 9 please review this page for consistency about dose being “applied” rather than “taken”.
5. Page 10: The Committee noted that there appeared to be emphasis on the risks of self-harm and suicide. The Researchers explained that previous open-label studies had not found increased risk of such side effects but that they had included this information due to cannabinoids being used. The Committee asked the Researchers to streamline the information by body systems e.g. physical reactions and mood reactions and state which are common to which are rare.
6. Page 10: The Researchers confirmed that the decrease in male fertility in animal studies while on the study drug was temporary and able to be reversed and the Committee asked that this be made clear.
7. Page 12: PedsQL Inventory – the Committee queried whether parents will be asked to answer questions about themselves and if yes, then they become participants in the study. The Researchers confirmed that the parents will complete the questionnaire for the children not for themselves. In the event that the information gathered does affect the parents then parents become participants and asked that the researchers add another statement in the consent form that states for parents that they consent to information about me being collected and used.
8. Page 13 under the heading ‘What are my rights?’: please also include comment that their child is also free to decline to be in the study at any time as the child has a right to dissent.
9. The Committee noted that if there is the possibility of mood reactions/side effects of the study drug then these need to be mentioned and also made known that the children will be assessed on regular basis for all adverse effects and what will happen to help if they happen.
10. Page 15, under the heading ‘Could this research be stopped unexpectedly?’: Please remove the statement “Decisions made in the business or commercial interests of the sponsor”.
11. Page 16. 4th paragraph under the heading ‘What will happen to information about the participant?’ The Committee asked whether the de-identified samples being sent to other countries is in addition to other samples that will be sent for analysis. The Researchers said no and that the samples will be analysed as a batch. The Researchers will seek confirmation about which countries the samples will go to.
12. Please remove the word “Retardation” and remove what FMR1 stands for and state “the gene implicated in Fragile X Syndrome” on page 2 of the information sheet.

Form for withdrawal of participation: the Committee noted that this can be done verbally and doesn’t have to be done in writing.

1. Sponsor clarify coming for follow up or for treatment. Need to have a taper period and dose reduction in this study. Not ideal to stop cold truly

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 check with the study sponsor and guarantee for the Committee that insurance is adequate. (*Ethical Guidelines for Intervention Studies* *paras 8.4 and 8.5*).

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

## 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:** | 28 August 2018, 12:00 PM |
| **Meeting venue:** | Room GC.3, Ground Floor, Ministry of Health, 133 Molesworth Street, Wellington, 6011 |

No members tendered apologies for this meeting.

The meeting closed at 4:15pm