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| **Committee:** | Central Health and Disability Ethics Committee |
| **Meeting date:** | 23 January 2018 |
| **Meeting venue:** | Room GN.6, Ground Floor, Ministry of Health, 133 Molesworth Street, Wellington |

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| **Time** | **Item of business** |
| 12.00pm | Welcome |
| 12.05pm | Confirmation of minutes of meeting of 28 November 2017 |
| 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 17/CEN/251  ii 17/CEN/271  iii 17/CEN/265  iv 17/CEN/267  v 17/CEN/270  vi 17/CEN/272  vii 17/CEN/273  viii 17/CEN/276  ix 17/CEN/277  x 17/CEN/282  xi 17/CEN/285  xii 17/CEN/286 |
| 5.30-5.45pm | General business:   * Noting section of agenda |
| 5.45pm | Meeting ends |

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

## Welcome

The Chair opened the meeting at 12.00pm and welcomed Committee members, noting that apologies had been received from Dr Patries Herst

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 28 November 2017 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **17/CEN/251** |
|  | Title: | COG ALTE1621 |
|  | Principal Investigator: | Dr Mark Winstanley |
|  | Sponsor: | Children's Oncology Group (COG) |
|  | Clock Start Date: | 11 January 2018 |

Dr Winstanley and Ms Paula Murray were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of ethical issues (resolved)

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

1. The committee queried whether there will be any reimbursement to participants for travel costs. The researchers explained that they are likely to target recruitment to people who live in Auckland who are coming in for standard tests and who could partake easily. Those people are usually reimbursed through the Ministry of Health and the researchers noted that if there is a gap then they can address this as they are not intending that participants be out of pocket.
2. The committee noted that the researchers had ticked ‘yes’ to questions ‘F’ and ‘H’ indicating that the exceptions for HDEC review applied. For future reference the committee noted that ‘no’ would have been the answers that applied. The researchers acknowledged that ‘yes’ was entered in error and that they would note this for future reference.
3. The committee noted, for future reference, that it would be useful at question p.4.1 in the application form that asks researchers to describe whether and how their study will benefit Māori to know the rate of Māori children receiving this type of chemotherapy. The researchers acknowledged this and advised that they would be more specific in the future. They did not have the numbers for cancer incidence and exposure to anthracyclines at their fingertips during the discussion for the benefit of the committee but acknowledged that they would attempt to be more specific in any future applications.
4. The committee queried the meaning of information stated at question p.4.2 that the researchers “engage in a dynamic consent process”. The researchers in attendance noted that the wording was another team member’s explained that it may have something to do with how time critical an enrolment process is. While this study is not a time critical one, in other trials researchers need to be available to do things outside of hours as they are often time critical.
5. The committee noted the submission of the CTSU short form for translation as standard consent and that the researchers are obliged to do this. The committee reiterated its stance that this form be used and signed after the main consent form is signed.

The committee requested the following changes be made to the participant information sheets and consent forms:

1. The committee asked that the researchers amend the footers on the information sheets and consent/assent forms to reflect the start date of the study.
2. The committee noted that it might be useful for the potential participants to know how many people have had the study drug before and whether it is commonly used or rare to be given to adolescents. The researchers noted that this is an interesting protocol patient group and that the medicine is not used on a regular basis. The researchers will consult with the cardiac team who will help with the study but were not at this meeting to give comment about prior use and in which patient groups. The committee noted that if the drug is rarely given then this knowledge may make a difference as to whether people choose to participate.
3. Page 9 under the heading ‘How long is the study?’: the committee queried whether the information about collecting follow-up information about a participant’s heart health for 3 years through their medical records meant follow up for 3 years in total or 3 years after they had finished their meds. The researchers advised that currently they have funding for a limited time period so they have identified 3 years from time of enrolment. The committee asked that they state this in the participant information sheet.
4. The committee queried whether participants will have access to the study drug after the study ends, for example if they are doing well. The researchers noted that the study drug is a medicine that is prescribed in New Zealand but there is currently no evidence that the medicine works – this study is looking to see whether this medicine works. If the study results are positive and participants wish to continue on the medicine then they could get access to it. The committee noted that it would be good to explain this to people in the information sheet – i.e if the drug is found to be beneficial it would be possible for you to get access to it after this study.
5. The committee noted the contacts stated on pages 10 and 11 and suggested that the researchers consider placing the contacts at the end of the document as a way of separating them out clearly for easy reference.
6. Page 14: the committee noted that there is provision for signature of participant (if aged 16+) and suggested the researchers change this to read “16 and over”.
7. Assent form for children aged 7-10 years: The committee noted the words “fake medication” stated under the title ‘What will I be asked to do?’ and asked that this be replaced with “pretend medication”.

Decision

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

The committee asked that the Secretariat review and approve the requested changes to the participant information sheet and consent/assent forms.

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| **2** | **Ethics ref:** | **17/CEN/271** |
|  | Title: | COG ALTE15n2 – LEAHRN Study |
|  | Principal Investigator: | Dr Mark Winstanley |
|  | Sponsor: | Children’s Oncology Group |
|  | Clock Start Date: | 11 January 2018 |

Dr Mark Winstanley 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 ethical issues (resolved)

The main ethical issues considered by the Committee were as follows.

1. The committee noted the letter of thanks for participation in this study and acknowledged the value but asked that ‘koha’ be removed as it is a token of thanks given to reciprocate time, knowledge and energy provided. Koha would normally be a voucher or food rather than a letter.
2. The committee queried whether travel time for participants will be reimbursed. The answer is the same as that provided for study 17/CEN/251 that it will be easier for the researchers to target participants who are in town, many of whom do a lot of follow up visits and the study would be done as part of this follow up so there would be no substantial change to the number of visits they make and they would not be out of pocket.
3. Question p.4.1 in the application form: the committee noted that it would be helpful to understand the incidence of late effects in Mãori children at question p.4.1 in the application form. The researchers noted that high risk neuroblastoma is a rare cancer with few patients nationally and that the sub analysis is going to be variable unless they have a large data set. The researchers acknowledged that this would be useful information to include in future.
4. The committee noted that the concept of ‘whakama’ for a Mãori child who has this cancer could be included as a cultural concern to consider and to acknowledge at question p.4.2 in the application form.

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

1. Page 2 of the parent/caregiver information sheet under the heading ‘What side-effects can I expect from being in the study?’. The committee noted the statement that if results of testing show concerning results that participants will be given further assessments or referrals for other care but doesn’t set out that the young person and their family will be told. The committee asked that the researchers include information that the participants will be told of any results.
2. The committee suggested that the researchers consider placing the contacts at the end of the document as a way of separating them out clearly for ease of reference. The researchers noted that they will talk with the team about consistency of approach in this regard.

Decision

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

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| **3** | **Ethics ref:** | **17/CEN/265** |
|  | Title: | Deprescribing Randomised Controlled Trial (RCT) |
|  | Principal Investigator: | Dr Hamish Jamieson |
|  | Sponsor: | University of Otago/Canterbury District Health Board |
|  | Clock Start Date: | 11 January 2018 |

Mr Ulrich Bergler 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 ethical issues (resolved)

The main ethical issues considered by the Committee and addressed by the researcher were as follows.

1. The committee noted that the main aim of the study is valuable and congratulated the researchers on winning HRC funding for this study.
2. The committee sought clarification on how some aspects of the study will work. The committee asked whether ‘vulnerable’ participants will be included in this study as information stated in the application form was not entirely clear on this point. At question O the researchers had stated that vulnerable people would be included in the study, then at question Ob that people with dementia or intellectual disabilities will be excluded but at the same time a range of older adults with impairments will be included. The committee noted that capacity to consent is a threshold and depends on the risks in the study and noted that this study seems low risk. The researchers advised that participants will be assessed by a clinician and inclusion criteria is that they must have capacity to consent. The committee then noted that the participant information sheet and consent form makes mention in a few places about a representative or relative being involved and asked for clarification about what the role of that person is. The researchers advised that the role would be one of support but that the participant alone will consent to taking part in this study. The committee asked that the researchers make clear in the participant information sheet that a person cannot give consent for another person (adult) to take part in research.
3. The committee asked how the prescriber or GP is included in the research process noting that the researchers had flagged in the application at question a.1.6 an ethical issue for the prescriber. The researchers explained that the pharmacist involved has done a similar study in Timaru in a rest home and that first communication about the study is with GPs by letter and in Christchurch the same approach will apply. In this study when the pharmacist sees a patient they will write a letter to the patients’ GP and then the person can discuss the study with their GP. The researcher confirmed that the patient would start reducing medication only after they have met with their GP. The committee queried whether the letter will advise patients not to stop taking their medication until after they have seen and talked with their GP and the researchers confirmed that this will be the case. The researchers confirmed that the ‘prescribers’ in the study are always GPs who manage routine medication prescribing. A participant’s GP will always make the call as to whether to reduce medication originally prescribed.
4. The committee queried whether the GPs are participants or co-researchers in this study. The researchers explained that the CDHB has adopted an approach where pharmacists review and make recommendations to GPs so there is a team approach to the research. The committee queried whether a person can still be involved in this study in the event that their GP doesn’t want to be involved. The researchers noted that they are not aware of this having happened in the past but if that happens in the intended study then they would not include the person.
5. The committee noted the mention of interview focus groups in the peer review submitted in this application. The researchers explained that the focus groups took place when they were developing a ‘frailty scale’ and that the focus groups are not relevant to this proposal.
6. The committee noted that it was satisfied that GPs are supporting the research rather than participating in the research themselves in the same way that a research nurse would be involved in a study.
7. The committee noted that information included in the application form suggests that patients in rest homes are involved but the participant information sheet submitted with this application doesn’t mention rest homes. The researchers confirmed that only people living in their own homes will be involved in this study and perhaps text from a previous study was included in this application. The committee asked that the researchers check this in future.
8. For future reference the committee noted that question p.4.2 asks for cultural issues to be identified and the concept of ‘whakama’ is a potential cultural consideration in this study as people may be embarrassed and ashamed to be losing abilities they have had.

Summary of ethical issues (outstanding)

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

Consent for use of health information for the control group: the committee noted that the peer review submitted with this application noted that seeking consent from the intervention group only was a violation of standard RCT design and may introduce a bias and that this is also an ethical issue that the committee will have responsibility to explore. The committee explained that in New Zealand when health information is used for a secondary purpose such as research, other than for what it was collected for, patients have a right to consent to this use. The National Ethics Advisory Committee (NEAC), guidelines provide at section 6.43 a process where an ethics committee can give a waiver to consent. The committee explained that there are a number of points that need to be addressed before a waiver is granted including that the requirement for consent would prejudice the scientific value of the study, the procedures required to obtain consent are likely to cause unnecessary anxiety for those whose consent would be sought and the public interest in the study outweighs the public interest in privacy. The committee noted that these points have not been addressed in the existing application. The committee noted that the researchers had stated in the application that people had consented as part of the interRAI and that there is some debate in New Zealand about that process with a diverse range of views held. In terms of the HDC Patient Code of Rights (Right 7), the committee’s view is that consent as part of interRAI does not count as consent as the person is not fully informed about this particular study. The researchers noted that they had debated about whether to use a control group as the controls don’t change medication load over time. The committee noted that comparison data could possibly be obtained via audit and used as a baseline and asked the researchers to think about whether they need a control group and if they do then in a response to the committee to address the requirements set out in the NEAC Ethical Guidelines for Observational Studies, para 6.43 for a waiver for consent: Access to identified or potentially identifiable data for research without the consent of the people the data identifies or makes potentially identifiable may be justifiable when: a) the procedures required to obtain consent are likely to cause unnecessary anxiety for those whose consent would be sought; or the requirement for consent would prejudice the scientific value of the study; or it is impossible in practice to obtain consent due to the quantity or age of the records; and b) there would be no disadvantage to the participants or their relatives or to any collectivities involved; and c) the public interest in the study outweighs the public interest in privacy. <https://neac.health.govt.nz/system/files/documents/publications/ethical-guidelines-for-observational-studies-2012.pdf>

The committee requested the following changes be made to the participant information sheet and consent form

1. The committee noted the document was overall well worded, clear and logical.
2. The committee noted that the document is 6 pages long but on page 2 of the document makes reference to pages 7 and 8.
3. Please add a footer that includes page numbers and version control on both the information sheet and consent form.
4. Page 2 under the heading ‘Initial appointment’, first sentence of the second paragraph: please review and simply this sentence.
5. Page 2 under the heading ‘What would your participation involve?’, first sentence: please replace the word “if” you choose with “before” you choose.
6. Page 2, last paragraph: The researchers confirmed that with the consent of the patient they will give a copy of the information sheet and signed consent form to a participant’s family member. Please make clear that the participant consents to this.
7. Page 2: please replace the word “human” and Disability Ethics Committee with “health”.
8. Page 3 under the heading ‘What would happen if you were injured in this study?’: please replace the statement with the following one so that it is clear that participants would be eligible to apply for compensation but that it is not automatically granted and they would need to be assessed:
   * *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.*
9. Page 3, 3rd paragraph that talks about the reason why a participant is feeling unwell. The committee queried whether a pharmacist will be qualified to say why people are unwell. The researchers confirmed that is not within a pharmacist’s scope of practice but if they can discuss adverse reactions linked to medication. The committee asked that it be made clear here that side effects may be due to the medication and if they are feeling unwell then they will be referred to their GP.
10. Please include contact details for a Māori support person who is independent of this study and is based locally. The committee noted that the office of the Health and Disability Commissioner does not provide Māori support and a separate number is needed.
11. Please make clear that participants don’t need to be on more than five medications to take part but that they do need to be on certain medications that make up drug burden.
12. Please make clear to participants what their commitment to this study will involve. The information sheet states that there is one main appointment, but does not say what the time commitment is. The researchers confirmed that some of the information about appointments/follow up visits are from the previous study and the committee asked that his information be removed.
13. In relation to what is expected of participants for study procedures and any associated risks please review the information you have provided at question r.1.1 in the application form and set this out in the information sheet for participants.
14. In relation to inclusion and exclusion criteria please revisit your answer stated at question f.2.2 in the application form and include and highlight it in the information sheet so that participants are sufficiently informed to make decision.

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 Angela Ballantyne and Dr Peter Gallagher.

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| **4** | **Ethics ref:** | **17/CEN/267** |
|  | Title: | enliGHten |
|  | Principal Investigator: | Prof Paul Hofman |
|  | Sponsor: | Pharmaceutical Solutions Ltd |
|  | Clock Start Date: | 11 January 2018 |

Prof Paul Hofman 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 ethical issues (resolved)

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

1. The committee noted that question a.1.6 in the application form that asks for a brief summary of ethical issues that may arise in the study was answered with information that there were no ethical issues. The committee noted that when a study is before the committee for consideration that there are ethical issues for consideration and noted that section ‘O’ in this application indicated that the study included vulnerable participants, trialling of a new medicine and standard treatment being withheld, which all raise ethical issues.
2. The researcher confirmed that this study will have SCOTT review.
3. The researcher confirmed that some of the participants in this study are patients and that steps will be taken to ensure that there is no conflict of interest. The CI will not recruit participants to the study.
4. The committee referred to question p.4.1 on page 28 of the application form that asks whether and how the study may benefit Mãori. The committee noted for future reference that it would have been helpful to include any known statistics on the incidence of growth hormone deficiency in Mãori to help inform the committee of how relevant this research is for Mãori.

The committee requested the following changes be made to the participant information sheets and consent forms:

Main Participant Information Sheet and Consent Form:

1. The committee noted that given the nature of the study that 18 pages of information seems excessive to ask participants to read this amount of information. The researcher noted that the company’s perspective is that they want people to understand everything and have provided a rigorous information sheet. The committee requested that all study visits be put in a chart or visual diagram for ease of reference and to avoid participants needing to read repeat information.
2. The committee noted that the comments it has in relation to the information sheet and consent forms are the same as for previous studies it has reviewed.
3. The committee noted that the documents had been submitted with comments and that the committee is meant to review the final document. In future the committee would like to see final documents without tracked changes or comments.

Main participant information sheet **and** consent form and Non pubescent years 12-15 assent form:

1. Page 9, information about the slipped capital femoral epiphysis: the committee noted that this condition could be an orthopaedic emergency for someone of this age group and that they are at high risk because of the treatment they are receiving. Please make it clear that they must contact their GP and or make sure that it is urgently assessed.
2. Page 9, information about Pancreatitis: please include fever and vomiting as primary symptoms. Please provide information that participants call 111 if this is an emergency.

Main participant information sheet and consent form:

1. Page 17: the committee noted that a parental consent form is provided for participants under the age of 16 and also for participants aged 16 and over. The researcher noted that it will recruit few participants aged 16 and over and even when the study is finished they will not be 16 years old. This study is a continuation of a currently approved study that has recruited boys under the age of 11 or and girls under the age of 12 for girls and in theory no one will be 16 years or older which is why the consent forms are done that way.
2. The information sheet notes that the sponsor could stop the study for commercial interest reasons. Please remove this statement as this is not an acceptable reason for stopping the study under NEAC guidelines.
3. Consent form for participants who are 16 and older: please remove the provision for Signature of parent/guardian as participants can legally consent for themselves.
4. Assent form for (non) pubescent years 12-15: please provide provision for the young person’s parents to sign.
5. Page 4: the committee noted the statement participants will allow the doctor to evaluate signs of puberty and asked whether the child will need to disrobe. The researcher advised that they will not need to do this and that these signs will be evaluated as part of standard physical checks. The committee asked that this be made clearer. i.e that they are doing a standard examination and that further checks will not be asked of them.
6. Please replace the compensation statements with the following statement which reflects that a person is eligible to apply for compensation:
   * 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, [x], 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.

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 Dean Quinn and Mrs Helen Walker.

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| **5** | **Ethics ref:** | **17/CEN/270** |
|  | Title: | Paracetamol vs combination analgesics for injury |
|  | Principal Investigator: | Mr Jiayi Gong |
|  | Sponsor: |  |
|  | Clock Start Date: | 11 January 2018 |

Mr Gong 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 ethical issues (resolved)

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

1. The committee noted its understanding that this study will look at the use of multiple analgesics in the emergency department to treat ‘moderate’ pain in limb injuries. The committee queried what a moderate pain injury would look like. The researcher noted that they wouldn’t know until an x-ray is done and that initially it would be based on pain scores (up to 10) and that they will do this study in patients with pain scores that are 3 and under. Moderate injuries will not include open injuries or anything that requires critical intervention. An ankle sprain in a match was given as an example of injuries that might be included.
2. The researchers aim to recruit 102 participants in New Zealand (51 patients in each arm) to allow for adequate statistical power in the results.
3. The committee noted that the peer review submitted with the study is brief but it does answer the questions asked. The researcher confirmed that the peer reviewer is independent of this study.

The committee requested the following changes to the participant information sheet and consent form:

1. Please include contact details for both a Māori support person and the Health and Disability Commissioner so that participants know that they have the option to make contact for support or with any questions they might have.
2. Please include ‘yes/no’ for statements that are truly optional. For example the last statement as this won’t impact on ability to take part in the study. GP consent can also stay as yes/no.
3. Please check that the footer and date and consent form proper are matching.
4. Under ‘What will my participation in the study involve?’ The committee asked whether participants will remain in the study if they are given additional pain medication. The researchers will follow them but the secondary end point measure will only include participants who have not received additional analgesics. The committee asked that the researchers add something along the lines of “do not hesitate to ask for more relief”.
5. Please include a statement that lets participants know they will be randomised and the ratios of tablets that they will receive.

Decision

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

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| **6** | **Ethics ref:** | **17/CEN/272** |
|  | Title: | Impact of HyperPhe |
|  | Principal Investigator: | Prof Suzanne Barker-Collo |
|  | Sponsor: |  |
|  | Clock Start Date: | 11 January 2018 |

Prof Barker-Collo 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. The committee asked the researchers for a precis of this research and in particular how they intend to recruit participants to the study.
2. The metabolic team see people diagnosed with Phenylketonuria on a semi-regular basis - around four times a year. Less regularly, once a year to 18 months, they also see people with HyperPhe. The researchers plan to recruit participants with HyperPhe in the first instance and want to have 10-11 cases to draw on. The hope is that the relationships they currently have with families will mean they can recruit 9-10 participants easily.
3. The next step will be to find participants with Phenylketonuria in full and under the management protocol who matched age and gender in the database who are being seen regularly and ask them at their next assessment if they are happy to be in this study.
4. Normal controls will be hard to recruit so the researchers are planning to contact families and use a snowballing effect to get matches in age and gender.

Summary of ethical issues (resolved)

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

1. The committee asked who will make contact with patients and non-patients initially. The researchers advised that the person will be a clinic staff member who usually phones to set up regular appointments and that person is not part of the study team. When they are contacted the staff member will ask them if they would like to have information about this study sent to them and when they come in for their regular appointment they will be able to ask any questions they have. The committee highlighted the issue of potential for coercion in someone who is a participant’s clinician as well as researcher consenting them to the study and noted that a way to work around this is to ask someone who is independent of the clinical team to consent participants. The researcher noted that a doctoral student who will do a clinical placement with the team could consent participants and the committee agreed that this would be ideal.
2. The committee queried whether the first mention of the study will be akin to a cold call and noted that it would be preferable to send an initial letter to potential participants so that they all have a chance to take part. In the event that all those contacted agreed to be in the study the researchers have the capacity to include this number.
3. The committee queried whether there is a possibility that the study is at risk of confounding by recruiting siblings. The researcher noted that any potential for confounding would be from those with PKU as they and their families have been on a special diet since the child’s birth. The other participants eat a regular diet and come into get a check. The main confound is in the behavioural aspects, as the PKU diet is so specific.

Summary of ethical issues (outstanding)

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

1. Consent vs assent: The committee queried why the researchers have taken the line of 14-15 year olds signing consent rather than an assent form. The researcher explained that they understood that 14-15 year olds are on the cusp in that they are old enough to understand the implications of this study but not old enough to legally give consent.
2. The committee explained that under current law in New Zealand that consent cannot be from two people simultaneously. In the case of this study parents will be consenting on behalf of children, AND that they get their child’s *assent* and therefore the child and has the right to say ‘no’. The committee noted that currently it is the role of the clinician to assess whether those who are under the age of 16 have the competence to understand the implications of the research and to consent an individual must be deemed to be Gillick competent. If the researchers choose to allow under-16s to consent for themselves they must have a process for assessing competence to consent.
3. The committee noted that the current information sheet and consent forms that span the 6-14 age groups is too wide noting that a 6 year old wouldn’t be able to understand the information and assent to being in the study. The committee suggests there is a smaller age interval for the assent forms to be in line with developmental reading and cognition levels and noted that pictures and diagrams are best for younger children in this case the age ranges of 6-19 and 11-15 would be appropriate. It was noted that Starship Hospital has good examples that the researcher might want to refer to

The committee requested the following changes to the participant information sheet and consent forms:

1. The committee noted that the parent/caregiver information sheet indicated there are no risks to being involved in this study pointed out that there are is potential to find cognitive issues in HyperPhe cases. Please include information about the potential risks.
2. Consent form: the committee noted that the statement about consenting to GPs or current providers being informed about participation and any significant results could be confusing for participants as the participant information sheet hadn’t included information about this. Please either remove or explain what they might be. Although these may vary the main ones would be cognitive and if there is potential to find adverse findings it is important to document this so that parents and participants are aware.
3. Page 2 under the heading ‘Possible benefits and risks of this study’. The committee noted the statement that participation in the study will stopped if harmful effects appear or if the doctor feels that it is not in the child’s best interests to continue. Similarly the doctor may at any other time give the child any other treatment considered necessary. The committee noted that the doctor can give treatment but only with their consent and asked the researchers define what you mean by harmful effects and then say something along the lines of if something unusual is raised then we will discuss with your doctor.
4. Page 2 under the heading ‘What will my participation in the study involve?’ The committee noted that the first paragraph as it stands is confusing and asked that the researchers set out clearly with bullet points that there are three groups – HperPhe, PKU and then control.
5. Please spell out how the control group will be recruited from the families and make clear what will happen. Please revisit the statement on the first page of the information sheets that says that there are “difficulties with thinking” in people with HyperPhe and PKU and present this in a more neutral way. The committee suggested that this could be said as something along the lines of there being “differences” in way they think and solve problems.
6. Under the heading ‘What will my participation in this study involve?’ The committee asked what the pen and pencil questionnaires involved. The researchers explained that they are distinguished from neuropsychology tests which are interactive. The committee noted that this would be helpful to say and asked that the researchers also give examples of what the questions might be.
7. Age appropriate pen and pencil questionnaires will be done by for parents and older children 11-16. Neuropsychology tests developed for 6 year olds – the tasks differ depending on age and are age appropriate.

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 Dean Quinn and Dr Angela Ballantyne.

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| **7** | **Ethics ref:** | **17/CEN/273** |
|  | Title: | Improving function of the pancreas and decreasing diabetes risk using a plant-polyphenol rutin |
|  | Principal Investigator: | Prof Sally Poppitt |
|  | Sponsor: | University of Auckland |
|  | Clock Start Date: | 11 January 2018 |

Prof Poppitt and Mr Wilson Yip 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 ethical issues (outstanding)

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

1. The committee noted the peer review submitted with this application addresses that this is an issue for NZ and other countries and noted its concern at the exclusion in New Zealand of particular populations. The researchers explained that the programme they are working with, the NSC\_HVN high value nutrition programme, has a particular focus on Asian/Chinese populations. The committee queried why there is a control group in this study. The researchers explained that there is interest in the whole programme to understand ethnic difference and do comparisons between the two groups. They noted that for type 2 diabetes in Asian populations even slim people seem to be at risk. In Caucasian, Mãori and Pacific Islander populations individuals can gain more weight before risks increase.
2. The committee noted that the title of the study submitted does not clearly reflect what the study is and its aims and also noted that it had questions about why this research excludes groups in New Zealand who are significantly affected by diabetes.
3. The researchers acknowledged this and noted that this particular programme has an Asian/Caucasian challenge. In this regard the committee noted that a related concern is the scientific basis for defining ethnicity in a meaningful way if participants are asked to self-identify. The researchers had planned to ask people to self-identify by identifying their parents in the screening questions. Participants would be excluded from this study if they cannot do this. Participants would also be excluded from this study if they identify their parents as being of mixed ethnicity. The committee asked what the definition of ‘Caucasian’ is. The researchers explained that they would expect participants to identify their parents as ‘NZ European’ in line with NZ census definition. The committee noted that that there is potential for ethnicity not to be captured accurately with the self-identifying approach. For example, it may be that the participant aligns ethnicity with one side of their parentage only.
4. The committee queried why a control group is needed when it does not appear that it would be a representative population. The researchers noted that this is because metabolic markers related to risk are different relative to adiposity and BMI so if they have a completely mixed population variability is larger and power calculations need to be larger.
5. Another question the committee had was regarding the benefit of this study and how the knowledge will be applied. Is the research looking just at an Asian population relative to European population or is it useful to know how an Asian population experience is relative to NZ population as a whole? In this study the comparison is between two groups rather than the wider population. The researchers noted that they do not have the funding currently to look at the population as a whole in this study. Within the programme there is no Māori and Pacific Island component within funding. The committee noted that it can see why there is a national focus on Asian populations in New Zealand but it was not clear on why Māori and Pacific Islanders are excluded. The committee also noted that it was not clear about how knowing the relative difference between two artificially designed populations will be useful to all New Zealanders. The researchers advised that they would hope or expect that the results are relevant to all New Zealanders but that they don’t have the funding to test this in this study. If they determined that interesting data is seen in earlier studies then it would be great to take it wider.
6. The committee noted that there is significant evidence to say that extrapolating results to other populations can’t be examined in a meaningful way. The committee noted that there needs to be a solid justification as to why Māori who are disproportionally affected by this condition are not included in the study.
7. The committee queried whether there is a different scientific way of answering the question. The question posed in the study is an interesting one but there is the challenge of control group that is not representative of a New Zealand population and has a sub population (Caucasian) that is difficult to define accurately as participants will self-identify by going just one generation back (to their parents). The importance of having a control group was noted but if the process of defining the control group is inaccurate then it calls into question the accuracy of any results. The committee noted that it would have been useful if the peer review submitted with this application had mentioned and commented on this as the committee don’t have expertise to assess it.
8. The committee asked whether it is necessary to have a control group in this study. It was suggested that the researchers could investigate this and have a look at the power and think about the numbers. In the study, as it stands, the control group isn’t a control group but a comparator group. If a control group is needed the researchers could think about how to use a control group that is representative of the general population.
9. The researchers noted that they have had other studies as part of the NSC-HVN Metabolic Health Programme ethically reviewed and approved through HDECs and those studies used a Caucasian comparator group. These studies were referenced at question p.3.1 in the application form. The committee agreed that it would like to review the HDEC assessments of those studies in comparison to the points raised in discussion of this application.
10. The committee agreed that it would decline this application to ask the researchers to resubmit an application for review at its meeting in February. In any subsequent application the committee would like to see a justification for not including Māori in this study along with peer review that provides a scientific justification for the exclusion of Māori and other population groups being necessary and that gives comment on the use of either a control or comparator group being scientifically valid. The committee will also use the time in between now and the next meeting to review the justification provided in the previously approved studies.

Decision

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

* Justice requires that, within a population, there is a fair distribution of the benefits and burdens of participation in a study and, for any participant, a balance of burdens and benefits. Accordingly, investigators must: design studies so that the inclusion and exclusion conditions for participants are fair. (*NEAC guidelines for intervention studies, para 4.5(b))*
* The study design should be the one best suited to answer the study question, while minimising harm, maximising benefit and meeting other ethical standards. *(NEAC guidelines for intervention studies, para 5.4)*
* Inclusion and exclusion of participants affect the extent to which study findings can be generalised. To contribute to an equitable distribution of study benefits and burdens, investigators should, when practicable, consider including all those who may benefit from the study findings. *(NEAC guidelines for intervention studies, para 5.27)*

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| **8** | **Ethics ref:** | **17/CEN/276** |
|  | Title: | Inhaled rifampicin proof of concept study |
|  | Principal Investigator: | Dr Jack Drummer |
|  | Sponsor: |  |
|  | Clock Start Date: | 11 January 2018 |

Dr Jack Drummer 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 ethical issues

The main ethical issues considered by the Committee were as follows.

1. The committee noted that this is an interesting study and asked whether this trial will involve the first time administering of this product via inhalation. The researcher noted that a previous study has used this mode of administration using a lower dose. There is some known safety data including data on dry powdered antibiotics.
2. The researcher confirmed that participants will be required to inhale the study drug under medical supervision at the centre, followed by a blood test and that they will not stay overnight in the centre. The committee asked that this be made clear in the participant information sheet and consent form.

The committee requested the following changes be made to the participant information sheet and consent form:

1. Page 2, first paragraph under the heading ‘What is the purpose of this study?’: the committee asked that the researchers reword to “when given as a pill” to “when taken orally” and to include information about the fact that there has been one prior study on inhaled rifampicin and some antibiotics are inhaled. Second paragraph: the committed asked that the researchers amend the statement “Rather than oral route, rifampicin given by inhaler will benefit TB patients by effectively killing the germs in the lungs” as this is not yet known as the study is being done to assess whether this is the case.
2. Page 3 under the heading ‘What if something goes wrong?’ please amend the ACC statement to read as follows:
   * *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.*
3. Consent form – please only include yes/no options for statements that are genuinely optional. Anything that is a requirement to be in the study does not need a yes/no option and in doing this it helps to make clear to participants what is compulsory and what is optional.
4. The 600mg control dose is a standard dose for people 60 kg and over and the researchers confirmed that this dose will be adjusted for participants who weigh under 60kg.
5. Page 3 under the heading ‘What are the possible benefits and risks of this study?’: please include that, although rare, anaphylaxis can occur and what will happen.
6. Page 3, point 1: please expand on this to include cigarettes and vaping products. Page 4 under the heading ‘What are my Rights?’ Please remove the word “practicable” as the HDC Patient Code of Rights allows people to withdraw at any time. If patient data collected up to the time a patient withdraws will be used, please state that here.
7. Please state in the information sheet that the person’s GP will be informed of their participation in the study and of any significant results gained.
8. Page 3, please replace the heading ‘who pays for the study?’ with ‘Will it cost me anything to take part?’ Please also change replace the works “incentives will be provided” to something along the lines of “you will be remunerated to recognise your time and involvement in the study” and that remuneration would be pro rata if a participant withdraws from the study for medical reasons.

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 Angela Ballantyne and Dr Melissa Cragg.

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| **9** | **Ethics ref:** | **17/CEN/277** |
|  | Title: | Heart-FID |
|  | Principal Investigator: | Professor Harvey Douglas White |
|  | Sponsor: | Luitpold Pharmaceuticals Inc |
|  | Clock Start Date: | 11 January 2018 |

Prof Harvey White 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 to the participant information sheet and consent forms:

1. For future reference the committee stated that it requires the final copy (that is, without tracked changes), of the participant information sheet and consent form as this is the final document is the document that it needs to know it is reviewing and approving.
2. Page 2, first paragraph: the committee noted that participants on the whole provide truthful information and try to provide researchers with the best possible information they have and don’t often set out to be deceitful. It might be more appropriate to say give your study doctor information that you believe to be true. Please include this information prior to the statement that the study doctor is being paid by the sponsor to conduct this research study.
3. The committee noted that information about patient responsibilities and study procedures is lengthy and asked in the interests of giving participants clear and helpful information that this information also be included in a table of study procedures. Inclusion of such a reference will make it easier for participants to work out what is going on.
4. Page 3, second paragraph – unclear of meaning, please think about using bullets. Could be a diagram if randomised, but if your iron level is okay then you don’t get further treatment.
5. Page 3 first bullet point under the heading ‘Participants’ Rights’: please simplify to state that you do not have to agree to participate if you don’t want to. Last bullet point: please simplify this statement to state that any complaint will be addressed.
6. Page 3 under the heading ‘Participants’ Responsibilities’: please amend the statement to say that you must be willing and able to walk for six minutes. Last bullet point: you can’t require people to stay in the study and the committee suggested that this statement be worded more softly to say while they are not required to stay in the study that the research team would like the participants to do so if possible. Say more softly we would like you to do this but shouldn’t be expressed this way.
7. Page 5 regarding treatment information. Please make clearer to participants who will do what – i.e that the study physician won’t know what treatment the participant is getting.
8. Page 8 under the heading ‘Possible side effects and risks of the study drug(s), placebo risks’ please make clear that if a condition does not improve or worsens that this is not due to taking a placebo alone.
9. Page 11 under the heading ‘Risks to breast fed babies:’ It is not clear if breast feeding is allowed during the study, please clarify within the PIS if breast feeding is allowed during participation in this study.
10. Page 12, second paragraph under the heading ‘Possible benefits of the study’: please remove the words “especially if you receive placebo”.
11. Page 13 and page 17, please replace the words “general physician” with “general practitioner” or “GP”.
12. Page 14, under the heading ‘Withdrawal from study’: please replace the sentence “very rarely your study doctor may need to stop participating in the study” with “very rarely the study doctor will have to stop participating in the study and another study doctor will step in”.
13. Page 17, third bullet point: the committee suggested that the word “abnormality” be replaced with something like “health issues” or “health concerns”.
14. The committee noted that the participant information sheet doesn’t say that samples will be sent overseas. If this is the case please include information so that participants are aware that their tissue 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*).

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

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| **10** | **Ethics ref:** | **17/CEN/282** |
|  | Title: | Comparison of the blood levels of two forms of alitretinoin 10 mg capsule in healthy male volunteers under fed conditions |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Douglas Pharmaceuticals Ltd |
|  | Clock Start Date: | 11 January 2018 |

Dr Noelyn Hung and Dr Tak Hung 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 ethical issues

The main ethical issues considered by the Committee were as follows.

1. The committee congratulated the researchers on a well completed application and noted that the application and participant information sheets were easy to follow and clear about is expected for participants. The committee had no ethical concerns in relation to this study and agreed to approve the application.

Decision

This application was *approved* by consensus.

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| **11** | **Ethics ref:** | **17/CEN/285** |
|  | Title: | AROAAT1001: A study of ARO-AAT in healthy volunteers |
|  | Principal Investigator: | Dr Christian Schwabe |
|  | Sponsor: | Arrowhead Pharmaceuticals Inc |
|  | Clock Start Date: | 11 January 2018 |

Dr Christian Schwabe and Ms Roselyn Shah 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 ethical issues

The main ethical issues considered by the Committee were as follows.

1. This study will investigate the safety and tolerability, in healthy volunteers, of a new treatment designed to treat alpha-1 antitrypsin deficiency. The researchers will investigate 5 different dose levels. Cohorts will receive single ascending doses and for safety doses will be escalated after day 15 when safety data is known for the prior cohort. As well as evaluating the safety and tolerability of the experimental treatment the researchers will look at the antitrypsin serum levels as this information will be helpful in designing the next phase which would be a patient one.
2. The committee noted that in future it would be good to know at question p.4.1 in the application form how relevant the research is for Mãori and with that in mind it is helpful for the committee to have any known statistics of the incidence of a condition in Mãori. The researchers noted that in general the condition is more common in European populations and the committee reiterated that such information would be useful to have included here. The committee also noted that Article 3 of the treaty is the article that talks about equality for Mãori.
3. The committee advised the researchers that in future it requires final patient information documents rather than documents with tracked changes so that it can be sure that it is approving a document that will not have changes made to it after approval.

The committee requested the following changes to the participant information sheets and consent forms:

1. Pregnancy PIS: the committee noted that an additional and consent form is needed for parents/caregivers to sign for measurements and information taken after the baby is born.
2. Future unspecified Research PIS: please revise the cultural statement on page 2 under the heading ‘How will you handle my blood samples after you collect them?’ For example blood is considered to be “tapu” not “taboo” and participants might like to obtain the blessing of their “iwi” rather than their “Mãori tribe”.

Decision

This application was *approved* by consensus.

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| **12** | **Ethics ref:** | **17/CEN/286** |
|  | Title: | LET vs VGCV for prevention of CMV in kidney transplant recipients |
|  | Principal Investigator: | Dr Ian Dittmer |
|  | Sponsor: | MSD |
|  | Clock Start Date: | 11 January 2018 |

Dr Ian Dittmer 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 ethical issues (outstanding)

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

1. The committee did not identify any significant ethical concerns but noted a number of small concerns on the participant information sheet and consent forms that it would like clarification on and that are noted below. The committee asked that the following points be addressed in a provisional approval response.
2. The committee noted the statement provided by the research team in regard to registration on clinical trial registry i.e that the researchers want to delay submission until a site is activated globally. The committee requested that the submission of a number once known will be a non-standard condition of approval before the study can begin. Please also include this number in the participant information sheets so that participants have access to a number to search for the study in the clinical trials registry.

The committee requested the following changes to the participant information sheet and consent forms:

1. Please include a table of study times and events to complement the four pages of information so that participants can have a reference point to more readily see what the study involves and what is required of them.
2. Page 4: second bullet point. Please provide more information to make clear what is meant by participants’ samples being used to study the link between variation in SLCO1B1 and UGT1A1.
3. Please clarify in the first bullet point that samples will be stored and used for the purposes set out in this information sheet
4. Page 6, last bullet point under the heading ‘Serious effects’: please clarify and or reword what is meant by “forceful behaviour”.
5. Page 7: please clarify for the committee why the statement “the below does not address risk language for the other approved indication of ganciclovir for the treatment of CMV retinitis in AIDS patients” is included. If this statement is not needed please remove it.
6. Page 13: please bold the words “50 years” in the statement that reads that participants permission to use and share health data about them will end in 50 years from the date they sign this form.
7. Page 14: please include contact details for a Māori support person. Please note that the HDC does not provide a support service for Māori and keep the HDC details separate from the Māori support person details.
8. Page 15, section 23: information about the optional samples for PK testing is brief – for example, it doesn’t set out what PK testing is, why it is being done in this study, nor how much blood will be taken and when (i.e at the same time they are giving other blood). Please provide a separate information sheet and consent form for this sub study.
9. PIS/CF for future unspecified research: please include the word “optional” in the title.
10. Page 2: please state that participants are being asked for consent to future unspecified use of their samples.
11. Page 3, first paragraph: please replace the words “to prevent others from finding out anything about you” with “to prevent the risk of someone finding out information about you”.
12. Page 4, section 9: the committee noted the statement “One way it might not be possible to find your samples is if the code linking them to the sponsor’s records has been destroyed at the study site”. The committee queried how often that happens and noted that if the records are retained for 20 years then the study sites are only able to destroy their records once the sponsor has agreed to that. Please clarify.

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 Dean Quinn and Dr Angela Ballantyne.

## 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:** | 27 February 2018, 08:00 AM |
| **Meeting venue:** | Room GN.6, Ground Floor, Ministry of Health, 133 Molesworth Street, Wellington, 6011 |

No apologies were tendered for this meeting

The meeting closed at 5.45pm.