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| **Committee:** | Central Health and Disability Ethics Committee |
| **Meeting date:** | 24 May 2016 |
| **Meeting venue:** | Room G.04, Ground Floor, Ministry of Health, Freyberg Building, 20 Aitken Street, Wellington |

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| **Time** | **Item of business** |
| 12:00pm | Welcome |
| 12:05pm | Confirmation of minutes of meeting of 26 April 2016 |
| 12:30pm | New applications (see over for details) |
|  | i 16/CEN/57  ii 16/CEN/59  iii 16/CEN/60  iv 16/CEN/61  v 16/CEN/63  vi 16/CEN/64  vii 16/CEN/65  viii 16/CEN/66  ix 16/CEN/67 |
| 4:15pm | General business:   * Noting section of agenda |
| 4:30pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Mrs Helen Walker | Lay (consumer/community perspectives) | 01/07/2015 | 01/07/2018 | Present |
| Dr Angela Ballantyne | Lay (ethical/moral reasoning) | 30/07/2015 | 30/07/2018 | Apologies |
| Mrs Sandy Gill | Lay (consumer/community perspectives) | 30/07/2015 | 30/07/2018 | Present |
| Dr Patries Herst | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | Present |
| Dr Dean Quinn | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | Present |
| Dr Cordelia Thomas | Lay (ethical/moral reasoning) | 19/05/2014 | 19/05/2017 | 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 12:00pm and welcomed Committee members, noting that apologies had been received from Dr Angela Ballantyne.

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 April 2016 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **16/CEN/57** |
|  | Title: | Na in CeD 3 |
|  | Principal Investigator: | Prof Richard Gearry |
|  | Sponsor: | Canterbury District Health Board |
|  | Clock Start Date: | 12 May 2016 |

No member of the research team was present for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This study investigates hook worms as a treatment for coeliac disease.

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 that the application form stated that there was not a risk of stigmatisation, however, although there may not be stigmatisation of coeliac disease that there may be stigmatisation from having a hook worm infestation as this may be associated with poor hygiene. The application form stated that this would not be a problem as no-one would need to know about the hook worm infestation, however, the committee noted that it may be possible for others to find out about the worms.
2. The Committee noted that the peer review provided was not ideal, as one of the reviewers is the CEO of the company and not independent, but that the study is being reviewed by SCOTT and this constitutes acceptable evidence of scientific peer review.
3. The Committee raised concerns regarding control participants, without hook worms, having endoscopies, and the increased risk this exposes them to. The reasons given for this was to maintain blinding of group allocation, and the Committee stated that this may be acceptable in this case as it is a participant’s choice to be involved in the study.

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 potential impacts on fertility from a hook worm infestation. The Committee requested further information regarding this, they understand that the reasons of the reduced fertility are unknown, however, they request more information on whether this only impacts female fertility, whether their fertility returns to normal after the infestation is removed, and request that any further relevant information is given to reassure the Committee on how this will be managed.
2. The Committee questioned whether it was possible for a cross infestation to occur. The Participant Information Sheet stated that in New Zealand and Australia it was not possible for the hook worm to spread to others. However, the Committee noted that if an infected person defecates outside or if the faeces from an infected person are used as fertilizer, eggs are deposited on soil and once matured can penetrate the skin of humans (such as if a person walks barefoot in contaminated soil). The Committee stated that it is possible that participants may defecate outside (if they are freedom camping or hiking) or they may use a composting toilet and that these practices may lead to the hook worms spreading to others. Please provide more information about the risks of cross infestation.
3. The Committee questioned whether there were significant risks associated with participants not taking the worming tablets at the end of the study, and choosing to maintain their hook worm infestation. The Committee noted that significant infestations could pose serious health risks to participants after the study and requested further information on this, including who would monitor these participants after the study. The Committee noted that they suspect that the low prevalence of hook worm and the low level of infestation mean that additional risks will only present if participants auto infect, however, they would like confirmation of this and reassurance that long term participants’ infestations will not get larger and pose more risks if they choose to not take the worming pill at the end of the study.
4. The Committee questioned whether it was possible for hook worms to be transmitted through sexual intercourse, such as if they have anal sex or participate in other activities that may increase their risk of transmission. If it may be possible for participants to transmit hook worms to their partners, please provide information about this, including whether their partners will be monitored during and/or after the study.

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

1. Please include a statement in the Participant Information Sheet regarding participant’s rights not to answer questions if they do not want to.
2. The Committee noted a lot of unnecessary legal language in the participant information sheet that may make this form difficult to understand, the Committee stated that these should be rephrased to improve clarity. For example, *“The New Zealand regulatory authority States that the New Zealand applicant/sponsor must ensure compliance with New Zealand privacy legislation and the Health (Retention of Health Information) Regulations 1996. In no case should the period of retention be less than 10 years from the date the study ends”* could be rephrased to read *“your health information will be kept for 15 years”* as the application form stated that this is how long health information will be retained in this study.
3. Please ensure that all unnecessarily technical information in the Participant Information Sheet is rephrased to ensure clarity for lay participants.
4. Please add inclusion and exclusion criteria to the Participant Information Sheet.
5. Please clarify in the Participant Information Sheet where samples retained for future unspecified research will be held, including whether this tissue bank is registered. The Committee noted that it appeared that the samples would be held in Australia, please confirm whether this is the case.
6. The Future Unspecified Use of Tissue Participant Information Sheet states that any future research will be approved by the Central HDEC. However, the Committee understands that samples will be stored in Australia and this suggests that future studies on these samples will be conducted in Australia. If this is correct, a New Zealand ethics committee is unlikely to review any future studies using these samples, and if these studies are reviewed by a HDEC if may not be the Central HDEC. Please rephrase this statement for clarity and accuracy.
7. The information sheet states that participants’ biological material or information derived from this will not be disclosed without the participant’s consent unless required by law. The Committee noted that the meaning of this statement is unclear and requested that it is clarified whether the future unspecified use of tissue forms cover this consent, or if they intend to re-approach participants to obtain consent to disclose their biological material or information derived from it.
8. The Participant Information Sheet states that participants must withdraw their consent in writing. However, in New Zealand verbal withdrawal of consent is legally binding. Please rephrase this section to ensure that it is clear that participants can withdraw their consent verbally.
9. Please include more information on the potential reduction in fertility from the hook worm infestation in the Participant Information Sheet.
10. Please include information on reducing the risk of cross infestation in the Participant Information Sheet.
11. Please ensure it is clear that all participants will have an endoscopy and be exposed to the risks associated with this.
12. Please include more information in the Participant Information Sheet about the risks associated with maintaining the participant’s infestation after the end of the study, including who is in charge of monitoring the infestation and possible health risks associated with this after the study.

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 respond to the outstanding ethical concerns detailed above.

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

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| **2** | **Ethics ref:** | **16/CEN/66** |
|  | Title: | Entyvio Extended Access Program in Ulcerative Colitis and Crohn'sDisease |
|  | Principal Investigator: | Prof Richard Gearry |
|  | Sponsor: | PPD Global Limited (New Zealand Branch) |
|  | Clock Start Date: | 12 May 2016 |

No member of the research was able to attend for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The Committee stated that they appreciated that this extension study would allow continuing access to the study drug to participants who are receiving a clinical benefit.
2. This study involves participants attending the study site every 8 weeks to receive an infusion of the study drug.
3. The extension study is being offered in countries where the study drug is not approved and/or subsidised as it would be difficult, or impossible, for participants in these countries to access the drug outside the extension study.
4. The Committee noted that this study will investigate the long term safety of the study drug.
5. The extension study will allow participants to have continued access to the study drug for the rest of their lives, unless they stop receiving a clinical benefit from it.

Summary of ethical issues (outstanding)

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

1. The Committee noted that the application form indicated that the researchers did not intend to publish study results in peer reviewed journals. Please provide more information regarding the reasons for this.
2. Please provide more information on the participants who have died in previous studies, including the percentage of participants that this represents and whether it is believed that these deaths are related to the study drug.
3. The Committee questioned the data safety monitoring arrangements for this study, as it appears that there is no formal data safety monitoring arrangement, please confirm whether this is correct and provide the justification for this.
4. The Committee noted that the application form referred to a detailed risk profile in the study protocol, however, the Committee was not able to locate this detailed profile and request that it is provided.
5. The Committee noted that the application indicated that data would be anonymous, however, a master list will be available for linking identifiable information to participant’s results as necessary. The Committee noted that this meant that data would be potentially identifiable, not anonymous. Please confirm if this is correct.
6. The Committee questioned how participants will be protected from coercion and how consent will be obtained. They stated that it appears that the lead investigator will be obtaining consent, and suggest that the risk of coercion would be reduced if someone else obtained informed consent as they would be less bias towards the study. Please provide more information regarding this.

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

1. Please rephrase the first sentence in the Participant Information Sheet to ensure clarity.
2. Please rephrase the Participant Information Sheet to reduce the risk of coercion, the Participant Information Sheet currently states a number of times on each page that participants are offered enrolment in the extension study as they are receiving a benefit and cannot continue to access the study drug outside the extension study. However, the Committee noted that the study drug is approved in other countries and could still be prescribed by participants GP’s if they are not in the extension study, although they would need to pay for this private access and it could be expensive.
3. The Committee also noted that the Participant Information Sheet currently has limited information on possible side effects and the deaths of people in the earlier studies. The Committee noted that these deaths may be unrelated to the study drug, or may be statistically irrelevant, however, this information should be provided to allow participants to make an informed decision about their participation in the extension study.
4. Please ensure that the Participant Information Sheet is clear that the study is to investigate the long term safety of the study drug, not solely to provide continued access to the study drug. It is important to include this information both to be transparent about the purposes of the study and to make it clear to participants that there is limited information on the long term effects of the study drug.
5. Please ensure it is clear in the Participant Information Sheet that although participants may receive a benefit from the study drug in the extension study that due to the limited information on the long term effects of this drug it is possible that its use may be harmful long term, they may develop side effects, and that the study drug could stop working.
6. Please remove the information not relevant to New Zealand from the Participant Information Sheet, for example be clear that the study drug is not approved or funded in New Zealand, and remove the mentions of spermicide from the contraception section as this is not available in New Zealand.
7. Please remove all mention, and option, for a legal representative to give consent or receive study results on the participant’s behalf. In New Zealand all adult participants must provide their own informed consent, and proxy consent, such as from a legal representative, is not acceptable.
8. Please rephrase the Participant Information Sheet to be clear about the timing of follow up visits, the Participant Information Sheet currently states that participants will have a follow up visit 18 weeks after the end of the study, however, participants may be enrolled in the study, and continue to have access the study drug, until their death, meaning that an 18 week post-study follow up is not possible.
9. Please proof read the Participant Information Sheet to remove unnecessary repetition and eliminate typographical errors.
10. The Consent form includes a statement regarding samples being sent overseas, however it is unclear from the Participant Information Sheet what samples this refers to. Please either remove this reference if it is included in error or provide significantly more information about the samples that will be sent overseas.
11. The Committee noted that the pregnant partner consent form currently provides for the pregnant woman to provide consent on behalf of her child before they are born. The Committee noted that in New Zealand it is not possible for a parent to provide consent on their child’s behalf before they are born. Please rephrase this Participant Information Sheet and Consent Form to reflect that the pregnant woman is providing consent to her participation, and consent to being contacted after the birth to provide consent for her child’s enrolment in the study. The Committee noted that as all of the relevant information is being provided to the pregnant woman in writing that it may be acceptable to obtain consent for the child’s participation verbally, over the phone, after birth to avoid the new mother and baby traveling to the clinic to provide consent. Please provide a revised Participant Information Sheet for the pregnant woman reflecting this, and details about how consent after birth will be obtained and recorded.
12. Currently the participant information sheets state that participants must withdraw their consent in writing, however, in New Zealand verbal withdrawal of consent is legally binding. Please rephrase the Participant Information Sheet to reflect this.
13. Please rephrase statements in the Participant Information Sheet regarding the possibility of pre-existing conditions being worsened by study participation, the Committee noted that the meaning of these statements is unclear as the condition cannot worsen if the participant does not have the condition, and that participants in this study will have Crohn’s disease. Specifically these sentences: “*worsening of Crohn’s disease in participants with Crohn’s disease”* and “*worsening of ulcerative colitis in participants with ulcerative colitis.”*
14. Please include that participants will be reimbursed for travel expenses in the Participant Information Sheet.
15. The Committee noted the reference to unexpected findings in the Participant Information Sheet, however, it is unclear what unexpected finding these could be as there is not an indication that blood tests are being done. The Committee suggested that this may relate to pregnancy testing, and if this is the case please rephrase this to improve clarity.
16. The Committee noted that the Participant Information Sheet lists Singapore as the local sponsor, however, this is not very local to New Zealand. Please confirm whether this is 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*).
* Please respond to the outstanding ethical concerns detailed above, please contact the secretariat if any clarification is required regarding these.

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

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| **3** | **Ethics ref:** | **16/CEN/59** |
|  | Title: | Determination of the Impact of Hepatectomy on Drug Metabolism |
|  | Principal Investigator: | Dr. Robert Matthew Strother |
|  | Sponsor: |  |
|  | Clock Start Date: | 12 May 2016 |

Dr. Robert Matthew Strother was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The Committee noted their appreciation that it is clear in the Participant Information Sheet that the partial liver removal is not part of the study.
2. The assumption from surgeons motivating this study is that patient’s metabolism of drugs is back to normal one month after partial removal of the liver, as the liver helps to metabolise some medications.

Summary of ethical issues (resolved)

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

1. The Committee questioned whether the study drugs are potentially harmful, especially in combination. The Researcher explained that they had minimal concerns about some of the drugs, that would be closely monitored, and no concerns regarding the rest of the drugs, especially at the levels they will be administered in this study.
2. The Committee questioned whether any statistics were available on liver resections in Māori. The Researcher explained that they were not aware of any statistics on this. The Committee noted that it would be useful to include this kind of information in any future applications.
3. The Committee noted that the question regarding cultural concerns in the application form should potentially discuss potential issues relating to whakama (shame), depending on the reasons participants are having part of their liver removed. The Committee noted that this was just for future applications.
4. The Committee questioned whether individual participants could benefit from study participation, such as by showing how the different drugs are metabolised in their body. The Researcher explained that the study results would not show any differences in metabolism between participants, it would only show if the individual participant metabolised the study drugs differently before and after the partial removal of their liver.
5. The Committee questioned whether any of the study drugs would have poor interactions with the drugs participants would receive following their surgery. The Researcher explained that they do not expect any interactions between the study drugs and the drugs administered as part of routine care.

Summary of ethical issues (outstanding)

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

1. Please be clear in the Participant Information Sheet that they do not know how “your liver” is functioning, rather than “the liver” as this suggests a broader lack of understanding than intended.
2. Please be clearer in the Participant Information Sheet regarding the possibility of receiving a copy of the study results, a tick box should be included in the Consent Form for participants to indicate if they wish to receive a summary of the study results.
3. The Committee suggested that the diagram from the protocol would be useful to include in the Participant Information Sheet.
4. Please alter the footnotes in study documents to ensure the correct study is referenced.
5. Please include in the Participant Information Sheet information regarding whether the study drugs are expected to interact with drugs administered as routine care, such as those administered during or after surgery.

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 Peter Gallagher.

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| **4** | **Ethics ref:** | **16/CEN/60** |
|  | Title: | EBC-46 in Patients with Refractory Cutaneous/Subcutaneous Tumours |
|  | Principal Investigator: | Dr Richard Stubbs |
|  | Sponsor: | QBiotics Ltd |
|  | Clock Start Date: | 12 May 2016 |

Dr Richard Stubbs was present in person and Dr Rodney Cusack and Mrs Stephanie Pollard 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 to allow him to remain in the room but not participate in the decision making for this application.

Summary of Study

1. This is a first in human trial, following animal testing of the study drug.
2. This study follows a dose escalation methodology, with the first, lowest, doses already having been done in Australia, the dose escalation will continue in New Zealand and Australia. One participant will be treated at each dosing level.

Summary of ethical issues (resolved)

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

1. The Committee questioned the data safety monitoring arrangements for this study. The Researcher explained that there is an internal monitoring committee consisting of all of the lead investigators for the study, primarily based in Australia, this includes 3 medical oncologists, a surgical oncologist, and a medical monitor who is also a medical oncologist.
2. The Committee questioned whether the medical monitor will visit the New Zealand study sites. The Researcher explained that the medical monitor is based in Australia and will primarily be in touch with New Zealand sites by phone.
3. The Committee questioned the extension study and whether all participants from this study will be offered enrolment in the extension study if the treatment has promising results. The Researcher explained that they hope to offer enrolment in the extension study to all participants who had a safe treatment in this study, and this will allow them to have multiple lesions treated, as in this study they can have a maximum of 3 lesions treated. The Researcher explained that the extension study would be a separate application, if a clinical benefit is found in this study.
4. The Committee noted that the application form states that study data will not be used for future research, they questioned if this is correct. The Researcher explained that this is a mistake in the form and the data will be used to inform future studies.
5. The Committee questioned how long participants had to consider their participation in the study after being presented with the Participant Information Sheet. The researcher explained that although participants would need to be treated within 2 weeks of the screening visit, they had longer before the screening visit to decide if they want to participate.
6. The Committee questioned why the researchers stated in their application that they did not need HDEC approval to use participant’s health information, as this is being used without consent for recruitment. The Researcher explained that this was a mistake in their application and they fully understood the reasons, and need, for obtaining HDEC approval.
7. The Committee questioned whether the safety review committee charter is still current as it is dated December 2014. The Researcher stated that this is still current as the study has been running in Australia for a while.
8. The Committee questioned how potential participants would be approached and recruited. The Researcher explained that interested participants would be referred by their treating clinician, after treatment with radiation had failed or been declined. Some participants may also be recruited through hospices, where the hospice workers would be informed of the study and able to mention it to patients who may be interested. Once potential participants have been identified and initially approached by their clinicians the consent process will be conducted by a member of the research team.

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 questioned whether potential participants would be given the research team’s contact details or if they would consent to having their details shared with the research team by their clinician. The Researcher explained that a brief information sheet or pamphlet would be given to interested patients who could use this information to contact the research team. The Committee stated that this pamphlet or information sheet must be provided to the HDEC for approval.

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

1. Please state in the first sentence of the Participant Information Sheet that this is a first in human study.
2. Please include some information about the previous studies in animals on the second page of the Participant Information Sheet, under what does participation involve, as although this information is later in the Participant Information Sheet it would be useful to also have some information in this section to explain the reasons behind the dosing levels.
3. In the section about what will happen in the study it may be useful to refer to the table included later in the Participant Information Sheet.

Decision

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

* Please provide the brief information sheet or pamphlet that will be provided to interested patients by their treating clinician to allow them to contact the research team.
* 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 Patries Herst and Dr Melissa Cragg.

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| **5** | **Ethics ref:** | **16/CEN/63** |
|  | Title: | Palliative Care for Pacific populations |
|  | Principal Investigator: | Dr. Sunia Foliaki |
|  | Sponsor: | Health Research Council of New Zealand |
|  | Clock Start Date: | 12 May 2016 |

No member of the research team was present for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This study is investigating how palliative care can be improved for pacific people, including investigating why they do not use this service.
2. The Committee stated that this research is important and they are pleased to see this application.
3. The Committee appreciated that participants would not just be given the Participant Information Sheet to read, they would be walked through this form with a researcher who would be able to ensure their understanding.

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 questioned whether the recruitment methods may bias the study results, specifically whether recruiting from palliative care providers would only result in recruitment of participants who are already accessing this service. The Committee noted that many patients with the most important results may not be involved with any palliative care providers, as they may be cared for in their homes by their families. Please provide more information regarding the rational for this and how it will be accounted for in the study results.
2. The Committee questioned how potential cultural factors would be accounted for. For example, the Committee noted that many pacific people tend to agree with people in authority, including doctors and nurses, even when they may not agree or have understood the question and will often say what the listener expects to hear. Please provide more information on how this will be accounted for.
3. The Committee questioned whether the researchers are obtaining cultural consultation for this study from a pacific group. The Committee suggested the working closely with pacific community groups would also allow for broader recruitment as these community groups will have the local family connections to identify individuals who are not accessing palliative care formally.
4. The Committee noted that many pacific people will provide palliative care in the home for their family members, rather than seeking formal support. The Committee suggested that this may be for many reasons including stigmatisation, pride, shame (such as if they are unable to provide the required care for their family members), and possibly a distrust of the establishment. The Committee noted that it is essential that the researcher is sensitive to these factors and that the questionnaires are appropriate. Please provide information on how this will be accounted for.
5. The Committee noted that family is central to pacific people and it is important that they feel involved in the process. Please clarify how this will be addressed, such as if the participant wants their family member to be present for their interview and to provide some answers to the questions.
6. The Committee questioned who would approach potential participants, they noted their preference that the initial approach is made by someone involved in their care and interested participants can then be referred to the research team.
7. Please provide a copy of any questionnaires that will be given to participants, and details of the kinds of questions that will be asked in interviews.

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

1. The Committee noted that although it is normally expected that the Participant Information Sheet will include a Māori cultural support contact number that in this case it would be more appropriate to provide contact details of a suitable pacific group that participants can contact with any cultural concerns.
2. Please include information in the Participant Information Sheet about the kinds of questions that will be asked to participants.
3. The Participant Information Sheet currently appears to only be directed at participants who are patients, however, participants will also be carers and family members. Please either adjust the Participant Information Sheet to ensure it is suitable for all groups of participants or create a separate Participant Information Sheet for each participant group as participation is different for each group.
4. The Committee suggested that the Participant Information Sheet could be rewritten to improve clarity, they suggested that the current study protocol is clearer and could be used as, or to improve, the Participant Information Sheet.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the committee *(Ethical Guidelines for Observational Studies para 6.10)*
* Please respond to the outstanding ethical concerns detailed above.

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

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| **6** | **Ethics ref:** | **16/CEN/61** |
|  | Title: | Dal-GenE Trial |
|  | Principal Investigator: | Professor Harvey White |
|  | Sponsor: |  |
|  | Clock Start Date: | 12 May 2016 |

Ms Carolline Alsweiler 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)

1. The committee commended the researchers on a well completed application.
2. The committee noted that the researchers have provided some good background and statistics for cardiovascular disease for Māori and pacific islanders. The committee noted that the researchers had stated ‘yes’ at question p.4.4 on the application form to the study involving kaupapa Māori methodologies. The researcher stated that they incorporate these aspects when dealing with site visits and are aware and sensitive to cultural standards. ‘Yes’ was in terms of site staff being for example, sensitive to whanau taking part.
3. The committee queried whether the researchers should have oversampled for Māori participation. The researchers advised that all sites screen all people with acute coronary syndrome so they anticipate that the proportion of those screened will be Māori.
4. The committee suggested that the researchers ask for local DHB support in recruiting Māori to the study. The Māori support people could go with the team and explain the consent process.

Summary of ethical issues (outstanding)

1. The committee asked how patients will be consented and what documents they will receive. The researcher explained that they were meeting with sites and discussing the process for study. One factor is that because they need to know the patient genotype before randomisation to the main study, they need to take a blood sample. 25 percent have the AA genotype and 80 percent will screen fail because of their genetic profile. At the screening stage participants will be offered a short consent only for taking of a sample from study doctor or research nurse. The hospital will screen admissions and then look for exclusion/inclusion criteria and approach eligible participants and discuss the taking of a sample for genotype screening and then patients will sign form to take sample. The committee queried why they can’t at the point of the initial approach discuss the whole study. The researcher thought that this would be best had discussion once genotype is confirmed. The researchers will then provide all the main study information at least a week before the genetic test results and will let participants know. Patients with AA genotype will be invited back for full consent process and receive full information about the study.
2. The committee queried whether this could be done in a different way and noted that as a participant at the point of the initial discussion about screening might like to know more about the main study and whether they’d be interested before giving samples for screening. There is a 1 in 5 to 1 in 6 chance of having the AA genotype and the study itself is randomised and placebo so they may only have 1 in 12 chance of getting the investigational drug and information about the main study this would be useful information to have at the point of consenting to screening.
3. The researcher explained that study coordinators when screening could explain a lot more about the study and give information and main consent and then consent just for blood sample and talk to clinician. The committee thought that would partly satisfy its concern that people need to know about the main study at the point of screening. The committee would prefer that either the volunteers being screened for the genotype are also given the main study PIS or that the PIS for the genotype screening needs to contain significantly more information about the main study – for example, the probability of receiving the study drug in the main study, the duration of the main study, etc.
4. The committee sought clarification on the use of the blood taken for the screening procedure that is going to be retained for 5 years to develop or improve testing. The committee asked what is meant by that statement and whether it is a back door approach to future unspecified research. The researchers noted that testing for market comes hand in hand with the screening genotype test. Participants with the genotype GG will be harmed (because they may have a worse outcome if they were to take the study drug), and other genotypes may derive no benefit. If they market then the genetic tests will also go to market and this needs to be validated and FDA approved. They still need to work on this process. If samples remain after screening then they may be used to commercialise.
5. The committee noted that the rule of thumb is that if testing occurs after a study finishes then it is ‘future unspecified research’. Such use is not going back and checking results and what the researchers intend to do could be anticipated as future unspecified research. The researcher offered to talk to the sponsor and ask for information about scope of testing on the samples. The committee noted that in the past it was happy with validation of a test but the working to commercialise might be considered FUR.

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

1. The committee noted that the information sheet is USA centric and asked that the researchers review it and amend so that it is more accessible to a New Zealand audience.
2. Please replace the word “subject” with the word “participant” throughout the document.
3. What the investigational drug is and how it works is not explained in the main information sheet. It currently talks about the genotype and how the drug might benefit but not about the drug itself and what it does – i.e. raise HDL-C levels. This information that the drug raises ‘good’ cholesterol levels could be included in the ‘Purpose’ section of the information sheet.
4. Page 3, ‘Nature of the Study’: the committee noted the first statement that participants are invited to participate because they are at high risk of having another cardiovascular event. The committee thought that some people might take that literally and think that they alone are at high risk. The committee asked that the researchers provide an explanation as to why the participants are considered to be at high risk.
5. Page 3, paragraph 4: The committee asked whether the researchers will tell the participant’s GP about the study results but not the participant themselves. The researcher noted that if the participant finds out that they are on placebo they may stop taking the study meds. The committee reminded the researcher of Right 6 of the Health and Disability Commissioner Code of Rights that people have the right to be fully informed of the results of tests and procedures and the right to ask their doctor for these. The committee asked that this statement be phrased slightly differently to comply with Right 6.
6. Page 4, ‘Subject’s rights’, third bullet point. Please remove the word “important” as it is redundant in this sentence.
7. Pages 4,5: Information sheet does not inform participants that their samples are going overseas for the tests. The researcher advised that the genetic tests will be at a US lab and a Singapore lab. Please ensure that this information is included in both information sheets.
8. Page 13, ‘Payment’: please replace the words “mass transit” with “public transport”.
9. Page 15, bullet point 6: please include general practitioner in this list.
10. Page 15: last paragraph: please remove the words “*and or to the person authorised to consent for the patient*”.
11. The committee queried the lack of a Māori tissue statement in the genetic Participant Information Sheet. The committee recommended the following statement: *You may hold beliefs about a sacred and shared value of all or any tissue samples removed. The cultural issues associated with sending your samples overseas and/or storing your tissue should be discussed with your family/whanau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult prior to participation in research where this occurs. However, it is acknowledged that individuals have the right to choose.”*

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 respond to the outstanding ethical concerns detailed above.

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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| **7** | **Ethics ref:** | **16/CEN/64** |
|  | Title: | Measuring the Length/Height of Children with Severe Cerebral Palsy in New Zealand |
|  | Principal Investigator: | Doctor Justine McCallum |
|  | Sponsor: | Starship Children's Health |
|  | Clock Start Date: | 12 May 2016 |

Dr Justine McCallum and Phillipa Clark 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 the study

1. This is an observational study measuring height and length of children with severe cerebral palsy in New Zealand. The two measurements used will be recumbent (lying) length using continuous segmental measures (from one bony landmark to the next) and the other is tibial length.

Summary of main ethical issues (resolved)

1. The committee noted the answer stated at question p.4.2 the main cultural issue for Māori in this study will be around the consent process as Te Reo may be a parent/caregivers first language so consenting in English will require careful explanation. The committee noted Whakama also and also ensuring that the child or whanau have a full understanding of what will happen.
2. The committee noted that the researchers had answered ‘no’ that Māori consultation is not needed at question p.4.3 on the application form. The committee queried why the researchers had answered no especially given that they had stated that the 2013 NZ Disability Survey found that Māori and Pacific people had higher-than-average disability rates. The committee noted that there is a likelihood of Māori being in this study and that the HRC Te Ara Tika guidelines provide that Māori are consulted in research that involves them. The researchers are proposing a new form of measurement and a level of consultation with their locality Māori research consultation group would be useful and may help the process to be more comfortable for Māori taking part. The researchers advised that they will go through the ADHB consultation process.
3. The committee noted that the researchers had stated at question f.1.2 on the application form that the study will improve the health of all children with cerebral palsy in New Zealand to the same degree and asked how the researchers know this. The committee noted that in this question it would have been good to see what would happen if the study generates knowledge that would reduce inequalities and then how or what extra measures the researchers have in place to ensure equal or population commensurate participation in order to inform study findings and results. This section should provide available statistics for Pacifica peoples, Asian people and other ethnic populations in New Zealand.
4. The committee noted that the scientific peer review submitted with this application raises the point that some children with severe cerebral palsy may find it difficult to do what the researchers are asking. Is it possible and if so then will it be uncomfortable for them. The researchers explained that they have been looking through the literature to see whether there are other ways they have done this. Older studies show children at the milder end of the spectrum can do this. Another method to use with children who have more severe form is known so there is a way around this.
5. The committee noted that the researchers had stated at question r.2.5 on page 16 of the application form data will be kept for 3 years. The committee reminded the researchers to ensure that all health information is stored for a minimum period of 10 years (Health (Retention of Health Information) Regulations 1996).
6. The researchers confirmed for the committee that they will not have any access to health information prior to gaining participant consent. They explained that schools will send a letter home in the school child’s bag that does not have any health information on it. If parents want their child to take part then they send the consent form to the research team.

Summary of ethical issues (outstanding)

1. The committee suggested that the researchers could have a short video clip that shows the child what will be done. The researchers thought that this was a good idea and possible ways in which the child could view this were discussed. E.g phone application that parents/caregivers could show to children. The researchers do not have the parents/caregivers contact details but they could give the school access to a video clip and give the parents the option of the viewing the video and sending them the main Participant Information Sheet.

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

1. The committee noted that it would be helpful if the assent forms for 7-11 year olds have pictures to illustrate what is going to happen and how the measurement was going to take place.
2. The committee noted that the researchers have submitted assent forms for 12-18 year olds and noted that 16 is the legal age of consent. The committee asked the researchers to amend this sheet so that it is for 12-15 year olds.
3. Parent/caregiver information sheet for Wilson centre participants: the committee noted that the first paragraph gives the impression that the researchers are looking at the possibility of children not growing properly when what they are looking at is the best way of measuring children with cerebral palsy. The committee suggested that the assent forms opening paragraph would make a better introduction.
4. Please include independent contact information for parents should they have any concerns or complaints about the study: If you want to talk to someone who isn’t involved with the study, you can contact an independent health and disability advocate on:

Phone: 0800 555 050  
Fax: 0800 2 SUPPORT (0800 2787 7678)  
Email: [advocacy@hdc.org.nz](mailto:advocacy@hdc.org.nz)

For Māori health support please contact :

*Name, position*

*Telephone number*

*Email*

You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Phone: 0800 4 ETHICS

Email: [hdecs@moh.govt.nz](mailto:hdecs@moh.govt.nz)

1. Please either change the last bullet point in each consent form to be consistent with the rest of the bullet points.

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 respond to the outstanding ethical concerns detailed above.

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

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| **8** | **Ethics ref:** | **16/CEN/65** |
|  | Title: | A Long-term Extension Study of PCI-32765 (Ibrutinib) |
|  | Principal Investigator: | Professor Peter Browett |
|  | Sponsor: | Quintiles on behalf of Janssen-Cilag |
|  | Clock Start Date: | 12 May 2016 |

Ms Sarah Dawes and Prof Peter Browett 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 the study

1. The researchers confirmed that there is one person in this study in New Zealand. Participants who were enrolled in a parent study that has now finished will be offered an extension to the treatment in order that they continue to have access to the treatment until it is accessible by doctor’s prescription and funded. In this study the researchers continue to collect long-term safety and efficacy data. There was only patient in NZ in the previous study and that patient has been offered an extension. The patient will continue to receive the study drug until they are no longer benefiting from the treatment (i.e. disease progression or toxicity occurs).

Summary of ethical issues (resolved)

1. The committee had no major ethical concerns about this study and the comments that it had were in relation to the participant information sheet and consent forms.
2. The committee discussed whether consultation with Māori was needed for this study given that one person will participate and that person is not Māori. The researchers explained that they sought consultation through the ADHB (Helen Wihongi) for the parent study that was open to all.

Summary of ethical issues (outstanding)

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

1. The committee noted that the participant information sheet and consent forms for this study are written in a way that is USA centric. The researchers stated that they agreed with this and that they would like to revisit the application and rewrite some of the information with this in mind and to make it more accessible to a New Zealand audience.
2. Please replace the word “subjects” with “participants”.
3. Page 2: Please include the word “worldwide” in the sentence “It is estimated that up to 200 subjects may participate in this study.”
4. Page 5, ‘What happens to the samples collected from me?’: The committee noted that the application submitted stated at question r.3.11 that tissue will be disposed of at the end of the study and that the wording in the information sheet suggests that samples may be used for future unspecified research. The committee asked the researchers to check whether the things listed will occur and if not then they should be removed from the information sheet. i.e. “identifying which people may respond differently to Ibrutinib” could imply genetic testing/pharmacogenetics and “developing tests for Ibrutinib and MCL, CLL and other haematologic malignancies” could imply future unspecified research – neither of these are covered by the current PIS/CF
5. Page 11, ‘What are the benefits of being in the study?’: the committee queried whether this statement could be moved forward in the information sheet given that there is one participant.
6. Page 11, ‘What other treatments are available?’: the committee noted that country specific, locally available alternative treatments/procedures were not stated here. The researchers confirmed that this is because the form is currently locked but that they would be able to update this.

Decision

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

* Please amend the information sheets and consent forms, taking into account the suggestions made by the committee *(Ethical Guidelines for Intervention Studies, para 6.22).*

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

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| **9** | **Ethics ref:** | **16/CEN/67** |
|  | Title: | Sleep and Health of People with Cognitive Impairment or Dementia and their Family Supporters |
|  | Principal Investigator: | Dr Rosemary Gibson |
|  | Sponsor: |  |
|  | Clock Start Date: | 12 May 2016 |

Dr Rosie Gibson 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)

1. The committee noted its concern that the researchers have indicated that they will include people who are unable to consent for themselves as research participants.
2. The Committee stated that it is not possible for HDECs to approve an application unless it is consistent with New Zealand law, including the right not to be subjected to medical or scientific experimentation without that person's consent (section 10 of the New Zealand Bill of Rights Act 1990). Research involving participants who are not competent to consent is inconsistent with the Bill of Rights unless it is undertaken in accordance with Right 7(4) of the of the Code of Health and Disability Services Consumers’ Rights. In addition to requirements regarding ascertaining the views of the consumer and other suitable persons (forms consistent with this aspect are currently included in this application), Right 7(4) of the Code requires that any health services provided without the informed consent of the consumer must be in the best interests of the consumer. This means that there must be some benefit, or potential benefit, to the participant beyond what they would receive if they were not participating in the research.
3. The researcher explained that some participants will be able to complete the form for themselves but others may have family members write for them if they cannot do so themselves. The committee accepted that there may be instances where the participant has impaired ability to write their own answers and in such cases then a family member or supporter could act as a scribe. However, the supporter or family member cannot consent on the participant’s behalf for the researchers to use data about them if they are not competent to understand what the study is about and consent for themselves to taking part.
4. The committee noted that it appears that the researchers would have the option to consent people with a mild degree of cognitive impairment or dementia who can consent for themselves and asked that only these people be included.
5. The committee noted that the information sheets talked about the issue sleep of “older adults” and they don’t recognise that a family supporter may not be older and may be a younger person. The committee asked whether younger people are excluded from taking part or whether all ages are included. The researcher stated that there are no exclusions based on age but explained that they had found in previous studies and older people tend to be in their client base and it would just be a case of rewording the information.
6. The committee noted that if its understanding in correct and if both the person with cognitive impairment and their family supporter will each complete the questionnaire then the researcher needs to give each participant separate and different copies of the information sheet and questionnaires as they need to be different between the two groups of participants and more clearly explain to both groups what participation entails.
7. Participant Information Sheet, Page 2, ‘What are the possible benefits and risks in participating?’: It is stated that some of the questions are of a personal nature and further explains what participants can do if they feel uncomfortable answering any question. The committee suggested that it would be helpful to give an example of the type of question that people might find uncomfortable here.
8. The committee queried the need for the questionnaire to ask for information about a participant’s salary, income, inheritance rights etc. and noted that such information shouldn’t be requested unless there is a reason that is relevant to the study for doing so. The committee sought clarification from the researcher about why they believe collecting such information is necessary. The researcher explained that this is a measure of social economic status and disease rates and they wish to capture differences in outcomes between ethnicities. The committee noted that the request for the information seemed intrusive and unnecessary.
9. The committee noted that the researchers are also asking the family support person to provide personal information as well and asked whether they will be asked to provide information about themselves or about the person they care for. It struck the committee as odd that the researchers are asking questions of the carers about their family member’s sleep when they may not observe them sleeping. The researcher explained that live in family carers only will complete the questionnaire. The committee noted that this needs to be noted in the participant information sheet as exclusion criteria and that they need to sleep in the same bed or the same room as the person that they care for.
10. Questionnaire, page 7: the committee noted that question 21 asks participants how often in the past month they have had certain experiences such as long pauses between breaths, legs twitching and of disorientation or confusion during sleep and noted that this could be difficult for participants to answer given that they will likely not know whether they are experiencing such events while they are asleep, (unless they were to wake up). The committee suggested that the researchers state the option of the participants asking their family support person or spouse about this if they are able.
11. Questionnaire, page 9: the committee noted that question 28 and the table there are hard to interpret. The researcher noted that they have used this questionnaire in previous research but have had the opportunity in that research to talk through the questionnaire with participants. Please revise this question so that it is clear to participants what they need to do.
12. The committee commended the response stated at question p.4.1 on page 18 of the application form that asks researchers to describe whether and how a study might benefit Māori. With this in mind the committee was interested to see that the researchers had answered ‘no’ the question p.4.3 that asks whether consultation with Māori is needed. The committee noted that the researchers will need to consult with Māori as part of their locality assessment process. The researcher noted that they will conduct the study at a number of sites and asked whether locality approval is needed for all sites. The researcher only needs to do locality assessment through the main site (Massey University) for this study.
13. The committee noted that the study contains potential cultural issues and that the researchers had stated “not applicable” at question p.4.2 that asks the researchers to identify cultural issues. While these issues will be raised in consultation, the application has not been correctly completed the committee suggested that the researchers seek guidance in completing their application. The committee suggested that the researchers might find the HRC Te Ara Tika guidelines a helpful reference.
14. Peer review has been provided from Alzheimers Wellington and the committee did not think that the peer reviewer in this case was the most appropriately qualified or independent person (as they are involved in the research) to have reviewed the protocol. The committee would like to see further independent review of the study protocol.

Decision

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

6.13 Investigators are responsible for designing and conducting studies to maximise the validity and quality of participants’ informed consent. Ethics committees are responsible for checking that proposed study information sheets and consent forms enhance informed consent of this nature.

6.22 Informed consent is essentially a matter of good communication between people. Information should be provided to potential participants in a form and in a way that assists their informed decision-making. For example, the information should as far as possible be provided in lay terms. In general, such information should:

1. explain the study, including:
2. the purpose of the study, including its expected contribution to knowledge and its potential benefits to communities
3. how the study meets the best intervention and equipoise standards
4. the purpose and practical significance of the use of randomisation, blinding or placebos, as relevant
5. the nature and sources of funding of the study, the institutional affiliations of the investigator(s), and who can be contacted to answer questions and how to contact them
6. the study’s status, with a current approval from an ethics committee
7. describe what the study involves, including:
8. what will be done in the study, including how participation in it will differ from not being in the study
9. the time involved in participation (eg, the number and duration of any visits to the research centre, and the expected finishing date of the study)
10. the purpose and expected number of any extra tests to be performed during the study
11. outline potential benefits, risks and compensation, covering:
12. foreseeable risks, side-effects, discomforts and possible direct benefits of study participation, including any risks or benefits to the health of a participant’s family members
13. arrangements for personal compensation for injury, including whether the study is covered by the Accident Compensation Act 2001
14. payments or other forms of reimbursement, if any, provided in recognition of participation
15. the extent of the investigator’s responsibility to ensure that care is provided to participants during the study
16. explain the rights of participants, covering:
17. the voluntary nature of participation, including that they are free to decline to participate or to withdraw from the research at any practicable time, without experiencing any disadvantage
18. the fact that participants have the right to access information about themselves collected as part of the study
19. the fact that participants will be told of any new information about adverse or beneficial effects related to the study that becomes available during the study that may have an impact on their health
20. what provision will be made for the privacy and confidentiality of individuals
21. describe what will happen after the study, covering:
22. whether any study intervention will be available to participants after the study and, if so, under what conditions (including any cost to them)
23. how study data will be stored and for how long, whether the data will be retained for possible future use, who will be responsible for their secure storage and how they will be destroyed
24. whether any biological specimens collected during the research will be destroyed at its conclusion and, if not, details of their storage and possible future use how the study findings will be communicated on completion of the study, including to participants, and in what expected timeframe.

## 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 June 2016, 12:00 PM |
| **Meeting venue:** | Room G.04, Ground Floor, Ministry of Health, Freyberg Building, 20 Aitken Street, Wellington, 6011 |

The following members tendered apologies for this meeting.

* Mrs Sandy Gill.

The meeting closed at 4:30pm.