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|  | ***Minutes*** |
| **Committee:** | Southern Health and Disability Ethics Committee |
| **Meeting date:** | 12 March 2019 |
| **Meeting venue:** | Sudima Hotel, Christchurch Airport, 550 Memorial Drive, Christchurch |

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| **Time** | **Item of business** |
| 11.30am | Welcome |
| 11.35am | Confirmation of minutes of meeting of 12 February 2019. |
| 11.45am | New applications (see over for details) |
|  | i 19/STH/34  ii 19/STH/44  iii 19/STH/46  iv 19/STH/47  v 19/STH/52  vi 19/STH/53  vii 19/STH/54  viii 19/STH/55  ix 19/STH/58  x 19/STH/59  xi 19/STH/60 |
|  | Substantial amendments (see over for details) |
|  | i 18/STH/240/AM01 |
| 4.20pm | General business:  Noting section of agenda |
| 4.30pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |  |
| Ms Raewyn Idoine | Lay (consumer/community perspectives) | 27/10/2015 | 27/10/2018 | Present |  |
| Dr Sarah Gunningham | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | Present |  |
| Assc Prof Nicola Swain | Non-lay (observational studies) | 27/10/2015 | 27/10/2018 | Present |  |
| Dr Devonie Waaka | Non-lay (intervention studies) | 13/05/2016 | 13/05/2019 | Present |  |
| Ms Sandy Gill | Lay (consumer/community perspectives) | 30/07/2015 | 30/07/2018 | Present |  |
| Assc Prof Mira Harrison-Woolrych | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | Present |  |
| Dr Paul Chin | Non-lay (intervention studies) | 27/10/2018 | 27/10/2021 | Present |  |
| Professor Jean Hay-Smith | Non-lay (health/disability service provision) | 31/10/2018 | 31/10/2021 | Present |  |

## Welcome

The Chair opened the meeting at 11.30am and welcomed Committee members.

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

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 12 February 2019 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **19/STH/34** |
|  | Title: | The impact of Plusoptix type autorefraction screening on amblyopia |
|  | Principal Investigator: | Mrs Sandi French |
|  | Sponsor: |  |
|  | Clock Start Date: | 31 January 2019 |

Ms Sandi French 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

National vision screening protocols done by the team have remained unchanged for some years now. Plusoptix type screening is replacing the use of vision charts in other countries. This study aims to do a comparison of both methods.

Summary of unresolved ethical issues

The main ethical issues considered by the Committee that require addressing by the Researcher were as follows.

1. The Committee sought clarification on a number of aspects from the application form submitted with this study.
2. Question a.1.6 asks for a brief summary of the main ethical issues the Researcher thinks may arise during the study. The Committee noted that the principal ethical issue is enrolment of young children into a research study who are considered vulnerable because they cannot provide consent, and may be on the borderline of being able to provide assent, to their participation in research. This has not been addressed anywhere in the application but should be discussed here.
3. The Committee noted the scientific basis for the study was not discussed in the application, and there was no reference to any previous research of Plusoptix in the paediatric population. A quick Google scholar search returned multiple papers about the use of Plusoptix in the paediatric population for amblyopia, including some where there appeared to be low specificity for certain types of amblyopia. The Committee queried whether previous research results had informed the current study design. For example, low specificity may impact on required sample size, and false positive tests may result in costs being incurred for parents / caregivers. The Researcher advised that Graeme Wilson probably has this knowledge, but acknowledged it had not been provided to the Committee to consider. The Committee noted that parents may also need this information before deciding whether or not to consent to their child’s participation in the study.
4. The study protocol did not adequately describe the study design or provide sufficient information about sample size for statistical validity (e.g. sensitivity and specificity tests). The Committee suggested that the Researcher seek some advice on writing a study protocol.
5. The Researchers have stated at question r.5.4.1 that there would be no conflict of interest between the service providers and the researchers. Ethically, where an individual is both a service provider and a researcher, he or she should carefully consider how conflicts of interest will be managed. The Researcher explained that consent for the additional screening for the intended study will be managed by the Researcher and will be a separate consent process to standard screening process. The Committee asked the Researcher to outline what steps they intend to take to ensure that parents don’t feel like there is any pressure on them to enrol their child in the study. The Researcher stated that this would be managed by information sharing through a community gathering at the early childhood centre. As this is part of the recruitment process, the Committee asked that this kind of information inform part of any subsequent application the research team makes to the Committee and to the rewritten protocol.
6. The researcher stated that the company that sell and market the camera will lend the device to the researchers for the study. The Committee noted that this needs to be declared and discussed in the application form and in the information sheet for participants.
7. In relation to the cultural questions around how the study might benefit Maori the Researchers have noted that they live and work in an area of high deprivation, where many are Maori. The Researchers are looking to address inequity gaps. The Committee asked how the Researchers intend to close the inequity gaps. The Researcher noted that she did not think incidence rates of amblyopia differed much between Maori and non-Maori.
8. Question p.4.3 of the application form is answered ‘no’ to indicate that consultation is not needed with Maori in accordance with HRC guidelines. The Committee noted that the guidelines provide guidance on research involving Maori and, that the purpose of consultation is to ensure that research contributes to Maori health development wherever possible. The National Ethics Advisory Committee Guidelines that the Committee is required to check are upheld also provide that issues relating to Maori cultural values should be addressed in discussion with Maori concerned. The Committee suggested that the research team refer to the HRC guidelines when further developing the design of their study.
9. In any subsequent application submitted for review the Committee asked the Researcher to include scientific peer review of the document completed by someone who is qualified to comment and who is independent of the study. A review template is available on the HDEC website and this has been sent to the research team.

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

1. The Committee thanked the researchers for using the HDEC pro forma, but noted that some of content not relevant to a study of this type could be removed. The Committee requested that the research team review the document with this in mind, simplify and rewrite in lay language.
2. The Committee asked the Researcher to reword the study title in lay language as it currently uses technical language.
3. The Committee asked the Researcher to revisit the information sheet and to write it for the child’s participation, not the parent/s’ participation. The parent will consent on behalf of their child but the language needs to reflect that it is the child who will participate.
4. Compensation section suggests that ensuing care required as a result of testing will be paid for. It currently states: “The professional screening and care your child will receive related to their participation in the study will not result in any cost to you or your child.” The Plusoptix procedure alone won’t cost anything and the Committee suggested that this be reworded to make clear that optometry referral / glasses / patching may incur costs to the family. For example: “If you are referred on then any costs associated with further investigations or diagnoses will need to be met by the parents as with normal care.”
5. Please clarify whether photographs taken are just of the eye or the entire face and please also provide more information about the photographs that will be taken – for example, are the images retained / stored? If yes, for how long? Can consent be withdrawn after the photograph is taken?
6. On the Consent form please provide space to enter the name of the child who the parent is consenting on behalf of.

Decision

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

* Please address how the study may benefit Maori and how cultural issues that arise for Maori participants in the study will be managed. (*Ethical Guidelines for Intervention Studies, para 4.7*).
* Please provide evidence of favourable independent peer review of the study protocol (*Ethical Guidelines for Intervention Studies, Appendix 1*)
* Please review and rewrite the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies, para 6.22*)

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| **2** | **Ethics ref:** | **19/STH/44** |
|  | Title: | The COAST pilot initiative |
|  | Principal Investigator: | Dr Amanda Sommerfeldt |
|  | Sponsor: | Southern DHB |
|  | Clock Start Date: | 28 February 2019 |

Laura Mulligan 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 outstanding ethical issues

The main ethical issues considered by the Committee that require addressing by the researcher were as follows.

1. The participant information sheets for both the health provider and the participant claim that the COAST form is a "universally accepted" form, and is "accessible to and accepted by all health care providers". The Committee’s understanding is that the COAST form is a new form and asked whether such claims are justified given the researchers are testing the new form to see if it will be acceptable.

The researcher explained that the feedback from previously held relevant stakeholder meetings had indicated that it would be a universally accepted form. Because this form is yet to be tested in a trial the Committee noted again that whether it is universally accepted is yet to be ascertained. The title and first paragraph of the information sheets are therefore leading and the Committee asked that the researchers reword the title and information sheet to more clearly state that a new form is being introduced.

1. The way in which the information sheet for the health professionals is written indicates their consent is being sought to participate in the survey element of the study only. The Committee queried whether consent should also be sought for their general participation in the study i.e. to use the COAST form. The Researcher confirmed that the intention is that the COAST form will be rolled out and used by all health professionals across Southland and only health care providers that give consent to be in the study will do the follow up survey. The ‘research’ aspect in this project is for use of clinician feedback/data from the survey.

The information sheet for patients in its current form states that “If you choose to participate your doctor or nurse will complete a COAST form.” This suggests that use of the form is contingent on the participants providing consent when this isn’t the case. The Committee suggested that the researchers reword the information sheet to make clear that the forms will be used whether or not a patient chooses to participate. The Committee suggested wording that clearly states that the patient’s doctor or nurse may be using the COAST form for quality assurance purposes and if they agree to participate then their information will be collected and they’ll be approached for a follow up survey.

1. The Committee made the general comment that the information sheet for the patient uses technical language throughout and raises sensitive and personal issues for someone who is in their last year of life. It was acknowledged that the clinicians will be talking with patients about these issues (e.g not to resuscitate), regardless of whether they choose to take part in this study. However, people often remember less than half of what has been said, may focus on certain words and remember incorrectly, and this information sheet will be what they take home to read again. With this is mind the Committee agreed that the information sheet needs more care and consideration put into the explanations about the purpose of the study and what their participation will involve.
2. In relation to the participants taking the participant information sheets home, the Committee noted that there is nothing mentioned about what the patient can do if they change their mind about what is recorded on the form. The Committee noted that it might be reassuring for participants to know that they will have the opportunity to revisit their decision over time. In other words reassure them that what they decide here isn’t final and they can revisit their decision with their health care provider over time. The Researcher explained that the research team had shifted their focus to the research aspect of data collection rather than completion of the form. The Committee advised the Researcher to include a statement that makes clear that the form is a clinical form and is going to be used as such.
3. The Committee noted that proxy consent for participants unable to consent for themselves has been mentioned in the main application form and the Committee reminded the Researcher that proxy consent for research is illegal in New Zealand. If researchers want to get the views of people who are providing proxy consent in a clinical setting (i.e filling out DNR forms in the usual clinical setting), then they have to be the primary participants in the study as well and they would have to give their own views about completing the COAST form themselves. If the researchers want to include these people in the study then a separate information sheet that sets out what they need to do is required.
4. The Committee noted the answer stated at p.2.9.on page 21 of the application form that the Researchers will not inform participants of the results of this study. The Committee’s expectation is that all participants involved in research in New Zealand have a right to receive the results of research that they are involved in. All participants need to be given the option of receiving a lay summary. Participants could be given this option on the consent form that the Researchers will ask them to sign.

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

1. Please include contact details for a Maori support person who is independent of the study and also for the Office of the Health and Disability Commissioner.
2. Please include footers
3. Consent form: please include yes/no boxes only for statements that are truly optional.

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 Observational Studies, para 6.10*)

This information will be reviewed, and a final decision made on the application, by Associate Professor Jean Hay-Smith and Mrs Raewyn Idoine.

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| **3** | **Ethics ref:** | **19/STH/46** |
|  | Title: | CBP-201AU002: Study of the Safety and Effect of CBP-201 in Adults with Atopic Dermatitis |
|  | Principal Investigator: | Assoc. Prof Marius Rademaker |
|  | Sponsor: | Connect Biopharma |
|  | Clock Start Date: | 28 February 2019 |

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

Potential conflicts of interest

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

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

Summary of study

A trial of a new drug in adults for treatment of moderate to severe Atopic Dermatitis. The drug has been used to treat other conditions but this is the first time it will be used in people with Atopic Dermatitis.

Summary of ethical issues

The main ethical issues considered by the Committee that require addressing by the Researcher were as follows.

1. The Committee noted the answer given at b.1.4 in the application form states this is a therapeutic study. However, the duration of treatment is just 4 weeks and there is a placebo arm. The Committee suggests the researchers revise this answer and, given it is a non-therapeutic trial involving an investigational drug, that the researchers consider providing appropriate payment to participants.
2. The answer given at p.3.1 suggests that researchers will recruit participants from among their patients. Please ensure that the initial approach regarding study participation is made by a member of the patient's usual clinical care team. If interest is expressed, the research team can then become involved.
3. The researchers have not answered the question in relation to study risks at r.1.1 in the application. There is risk to participants given they are being asked to stop their standard treatments. The most important / common risks of the study drug should be included in this section. Please outline these and what steps will be taken to monitor / manage any important risks.
4. The Committee queried whether one of the exclusion criteria was no access to internet as the application indicates that participants will be required to use their own devices to access the internet.
5. The Committee noted the information provided in relation to consultation with Maori is lacking. The purpose of consultation is to ensure that research contributes to Maori health development wherever possible. No information is given about the incidence rate / prevalence of Atopic Dermatitis in Maori and how this compares with the rest of the NZ population at question p.4.1.
6. The National Ethics Advisory Committee Guidelines that the Committee is required to check are upheld also provide that issues relating to Maori cultural values should be addressed in discussion with Maori concerned. The cultural issues for Maori at p.4.2 have not been addressed in full. For example, use of tissue for research purposes is a significant issue for many Maori.
7. Question b.4.3. The HDEC does not have access to the CTA. Please summarise the publication restrictions that are in place.
8. Question b.4.4.1 In general data made available to other researchers should at a minimum be de-identified. Please provide justification for providing data generated by the study to other researchers in potentially identifiable form.
9. Question r.1.1. Is 2 hours of observation post first dose of a subcutaneously administered monoclonal antibody with limited human exposure sufficient? How was this time period selected?
10. Question r.1.3.1. Will a discussion take place with each participant's GP / specialist prior to any standard of care therapy being withheld for study purposes?
11. Question r.3.1.2. States all samples will be destroyed once analysis is completed. Is there no plan for back-up samples to be retained in the event re-analysis is required?

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

1. Please review the information sheet and consent form and rewrite in lay language. The documents as they stand repeatedly use technical language. E.g. “tolerability”.
2. Please provide a lay schedule of assessments table.
3. Please state upfront on page 1 that this is the first time multiple doses of the drug will be tested in humans, and the first time the drug will be tested in people with atopic dermatitis.
4. Please state on page 1 that the study is being run for the benefit of Biopharma.
5. The information sheet mentions “testing a new treatment” which is leading as it is an investigational or trial drug at this stage. Please reword this statement. Please state that the drug is not approved for treatment of Atopic Dermatitis “anywhere in the world”.
6. The reproductive risks information is not adequate. Please see the HDEC guidance on information to include in relation to reproductive risks at: <https://ethics.health.govt.nz/guides-templates-forms-0/participant-information-sheet-templates>
7. Total blood volume to be taken is stated as 245ml. The Committee suggested that this be checked as it has also been stated that 103ml will be taken at each of the four times participants receive the drug plus extras.
8. Tuberculosis is notifiable to the Ministry of Health in New Zealand and this needs to be added to the section about HIV / HBV / HCV. The type of test(s) used to screen for TB in this study should be specified.
9. Risk section: please state that there is the risk that their condition might worsen given they are stopping standard treatment. The Committee would also like to know whether discussion will be had with the participant’s GP prior to stopping standard treatments.
10. Withdrawal information discusses the use of data but not use of samples. Please state whether remaining samples will be destroyed or whether collected samples will continue to be analysed.

Decision

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

* For participants in an intervention study, the overall benefits and risks of the intervention being studied are uncertain. This study will assess an investigational drug thought to be an improvement over current standard of care, but the participant may or may not benefit from the intervention. There is also the potential for harm. To be ethically sound, the risks and benefits must be weighed and the application and information sheet as currently submitted do not inform the Committee nor the potential participants for the risks of withholding standard therapy, risks of drug withdrawal in coming off standard therapy, or having placebo after being on standard treatment.
* The Committee did not have enough information before it to determine whether the intended study meets the requirement set out at *para 5.49 of the Ethical Guidelines for Intervention Studies*, which provide: a non-therapeutic intervention study is justified only when the importance of the objective outweighs the inherent risks and burdens to the participant, and participants are well informed of the possible risks.

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| **4** | **Ethics ref:** | **19/STH/47** |
|  | Title: | Developing Potential New Treatments for Epidermolysis Bullosa |
|  | Principal Investigator: | Dr Hilary Sheppard |
|  | Sponsor: | The University of Auckland |
|  | Clock Start Date: | 28 February 2019 |

Dr Hilary Sheppard 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 resolved ethical issues

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

The Committee recalled the Researcher’s previous application and thanked her for her efforts in resubmitting the application before the Committee today.

1. There were previously several key ethical issues, which resulted in this study being declined, but these have now been resolved as follows:

1) Participants under age 16 years. The researchers have now limited this study to those age 16 years above and will seek informed consent from all participants. There is now one adult-appropriate participant information sheet.

2) Scope of conditions investigated. The researchers have now restricted this study to EB and this is specified in the participant information sheet.

3) Inclusion of Maori participants. The committee was previously concerned that Maori were excluded from this study. The researchers have now included Maori and this has been approved by their local Biological Safety Committee.

4) Lack of expertise in gene editing and other scientific peer review concerns. The researchers now have a UK expert named on this project and have provided some evidence of scientific peer review. It is not detailed, but the scores are satisfactory.

5) Inclusion of information about skin biopsies. More detail has been included about the biopsy procedure, with actual size diagrams. The risks of scarring and infection have also been included and participants will be given wound-care instructions to minimise these risks.

The Committee sought confirmation that all biopsies performed in this research will be done by registered health professionals. Under New Zealand law only registered health professionals may do biopsies. The researcher assured the Committee that only registered health professionals who are appropriately qualified will do the biopsies.

Participant information sheet, page 4, under the description of how the muscle biopsy will be done. Please include two subtitles: ‘Skin Biopsy’ and ‘Genetic Editing’ to separate the two for the participant.

6) Information for participants on genetic procedures The PIS now has sub-sections about genetic testing (only in those who have not had any) and genetic modification procedures, including the use of animals. These sections are generally well explained, but the Committee asked that the Researchers re check this section for over-use of technical terms e.g. PCR

7) Storage of tissue after study Samples will be kept and may be used for up to five years. There is an option to consent to use of cells for up to 15 years. The Committee accepted this given that the Researchers have clearly stated it in the information sheet and consent forms.

8) Other PIS issues. The new PIS is much improved and includes readable detail about all the above issues, appropriate ACC statements etc. There is also information about data collection from medical records in relation to the study.

1. The Committee noted the statement that treatment would not be given at question r.1.7 on the application form. This is incorrect as punch biopsies administered by health professionals are considered treatment in this context. Therefore the Committee needs to see that the Researchers have addressed questions around compensation in event of injury. The Committee asked whether or not the study is being principally done for the benefit of the distributor or manufacturer. The Researcher explained that they are not creating a product and the study is purely preliminary research and therefore ACC cover applies in the event of treatment injury.
2. The answer given at question r.3.3 on the application form states human stored tissue samples will not be used, however earlier in application states 'where previous histology blocks exist we would like permission to use these'. If this is intended, a number of questions should have been populated and answered. The researcher confirmed that answer was incorrect and they are now not going to be using previous histology blocks.
3. The Researcher confirmed that the initial approach to patients would be made by a member of the patient's clinical care team. If interest is expressed the research team may then make contact.

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

1. The Committee noted the statement: "participants will be selected by Dr Diana Purvis" Please rewrite this to state that participants have been invited to take part in the study because they have a diagnosis of EB.
2. The Committee queried the lack of a Māori tissue statement in the Participant Information Sheet. The Committee recommended the following statement: “*You may hold beliefs about a sacred and shared value of any tissue samples removed. The cultural issues associated with sending your samples overseas and/or storing your tissue should be discussed with your family/whanau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult prior to participation in research where this occurs. However, it is acknowledged that individuals have the right to choose.”*
3. The Committee noted the statement “We do not plan to transplant modified cells onto you or anyone else at this time and the genetic modifications we introduce cannot be passed on to any children.” appears to be contradictory as no modified cells are being introduced and therefore they can’t be passed on. The Committee suggested that the statement be shortened to “We do not plan to transplant modified cells onto you or anyone else at this time.”
4. The Committee noted its expectation that individuals who participate in research have the right to receive a lay summary of study results and it noted that participants usually have a keen interest in the outcomes. Please ensure that all participants are given the option of receiving a lay summary of study results. The option (yes/no) can be included in the consent form.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* paragraph6.22).

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| **5** | **Ethics ref:** | **19/STH/52** |
|  | Title: | M16-011 |
|  | Principal Investigator: | Dr Marina Sew-Hoy |
|  | Sponsor: | AbbVie Pty Ltd |
|  | Clock Start Date: | 28 February 2019 |

Ms Larissa Roberts and Dr Nigel Gilchrist 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

This study is very similar to 19/STH/53 also considered at this meeting, with a slight difference in patient population. The study will look at a new IL23 monoclonal antibody to treat psoriatic arthritis that has inadequately responded to previous therapies.

Summary of ethical issues

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

1. The response to r.1.13 in the application form states that there will no additional ionising radiation, however it is noted in the information sheet and consent forms that x-rays are required at regular intervals during the study. These would appear to be more frequent than they would under standard of care. The Researcher advised that with this sort of agent they believe that the slightly increased frequency of x-rays would be within the standard of care. The Committee noted the information sheet has a ‘risks’ section that includes information about the x-rays and asked the Researchers to remove this information given the x-rays will with within the standard of care.
2. The Researcher confirmed that the first approach to potential participants will be made by a member of the patient's clinical care team.
3. The use of placebo in those with significant active disease does not appear to have been justified at question f.2.3.1. The Committee is looking for a justification of why it is okay to give half of the participants’ placebo for the first 24 weeks of the study. The Researcher advised that it is implicit in the study design (double-blinded, randomised trial), and that participants will also be on other drugs and have access to other pain medications as well as anti-inflammatory medications. They will carry on with usual treatment.
4. The questionnaires submitted with the application ask questions about depression yet there is no safety plan outlined in the study protocol that talks about what researchers will do should they find a participant has depression. Who will check and collate the information given in the questionnaires?

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

1. Please provide a lay title for the study.
2. While the documents are comprehensive the Committee noted some sections could have been ordered differently. For example in the risk section the most important information should be stated first – i.e. the risks of the new medicine.
3. The reproductive risks section notes products that aren’t available in New Zealand. Please see the reproductive risks guidance on the HDEC website and use this information. <https://ethics.health.govt.nz/guides-templates-forms-0/participant-information-sheet-templates>
4. In general there are terms such as 'efficacy' / 'anaphylaxis' / 'connective tissue' that aren’t defined and aren’t often well understood by lay people. The Committee asked the researcher to review the document and replace some of the terms with lay terminology where necessary.
5. Page 2, para 5 reads like a legal document. Please simplify or remove this information.
6. The study’s activity table has a number of assessments have provisos "per local regulatory guidelines". Please find out what actually applies in the NZ setting, and use specific information or delete when not applicable in New Zealand. This applies, for example, to demographics/Tuberculosis screening/Hepatitis and HIV screening. Also note Tuberculosis is notifiable in New Zealand.
7. Page 10, under the heading ‘What are the possible risks of being in this study?’: please remove the reference to inserting EC information.
8. Page 17 second to last para. Information in relation to coded data talks about internal privacy agreements and transfer of coded data. Terms such as 'internal privacy agreements’ and 'international data transfer restrictions' provide no useful information to most people. Please either explain in simple terms or delete.
9. In the optional biomarker research participant information sheet and consent form please make clear that the samples are being used for research into psoriatic arthritis.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* paragraph6.22).

This information will be reviewed, and a final decision made on the application, by Ms Raewyn Idoine and Dr Devonie Waaka.

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| **6** | **Ethics ref:** | **19/STH/53** |
|  | Title: | M15-998 |
|  | Principal Investigator: | Dr Marina Sew Hoy |
|  | Sponsor: | AbbVie Pty Ltd |
|  | Clock Start Date: | 28 February 2019 |

Ms Larissa Roberts and Dr Nigel Gilchrist was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of study

1. This study is very similar to 19/STH/52 also considered at this meeting with a slight difference in patient population. The study will look at a new IL23 monoclonal antibody to treat psoriatic arthritis that has inadequately responded to previous therapies.
2. Please refer to minutes for 19/STH/52 as the discussion and information requested also applies to this study.

The Committee requested the following changes to the participant information sheets and consent forms.

1. Please see minutes for 19/STH/52.
2. Optional biomarker research participant information sheet, page 1 , first paragraph under ‘What is the purpose of the optional research?’ reads as though a patient who fails csDMART but hasn’t tried biologics could be enrolled in this study whereas the information sheet title states failure with biologic therapies, not csDMARDs. Please clarify.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* paragraph6.22).

This information will be reviewed, and a final decision made on the application, by Ms Raewyn Idoine and Dr Devonie Waaka.

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| **7** | **Ethics ref:** | **19/STH/54** |
|  | Title: | SAGE-ANZ |
|  | Principal Investigator: | A/Prof Rachael Parke |
|  | Sponsor: |  |
|  | Clock Start Date: | 28 February 2019 |

A/Prof Rachael Parke 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

Little is known about therapies or survival outcomes for this patient group while they are in intensive care. The Researchers would like to prospectively collect patient medical data for a period of six months. In particular they would like to collect data about what therapies were used and also daily oxygen levels, type of ventilation and settings used. Once collected the Researchers would like to compare with data collected in the USA to look at regional variations and also to inform trial design for ventilation strategies to test to see if outcomes can be improved for this patient group.

The Researchers are going to collect information that would be collected as part of standard clinical care and do not intend to collect additional data points. The Researchers chose a prospective collection of data rather than retrospective collection of data because they believe this will lead to a more complete dataset.

Summary of ethical issues

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

1. This study involves the prospective collection of and secondary use of health information for research purposes, without consent. This patient group will be unconscious and on a mechanical ventilator at the time the data is being collected and therefore they cannot provide consent.
2. The Committee explained to the Researchers that it is not able to approve an application unless it is consistent with New Zealand law. Research involving participants who are not competent to consent is inconsistent with New Zealand law 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 must be included with the 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 Committee notes that proxy consent is only legally acceptable in cases where the medical experiment would save the person’s life or prevent serious damage to the person’s health. Therefore, documents for ascertaining the views of the participant’s family, or other suitable persons, should only be used to gauge the views of suitable persons regarding whether the potential participants would want to participate if they were able to consent for themselves. This means that the forms should not involve language whereby the participant’s relative/friend/EPOA consent on their behalf. This is in line with Right 7(4)(c)(ii): *If the consumer's views have not been ascertained, the provider takes into account the views of other suitable persons who are interested in the welfare of the consumer and available to advise the provider.*
4. Once reasonable steps have been taken, the clinician may be able to enrol participants unable to provide informed consent, provided that study participation is deemed to be in the participant’s best interests.
5. Given the nature of the intended study the Committee noted that it is likely that the study could not be argued to be in each participant’s best interest nor would it be likely to save the person’s life. As the data is collected as part of standard clinical practice the Committee suggested that the Researchers could get the information they need by collecting it retrospectively from medical notes.
6. If the consent is unable to be obtained for the retrospective collection of data from patient notes the Committee could consider a waiver for consent if the researchers could justify that:
   * 1. *the procedures required to obtain consent are likely to cause unnecessary anxiety for those whose consent would be sought; or the requirement for consent would prejudice the scientific value of the study; or it is impossible in practice to obtain consent due to the quantity or age of the records; and*
     2. *there would be no disadvantage to the participants or their relatives or to any collectives involved; and*
     3. *the public interest in the study outweighs the public interest in privacy. (Ethical Guidelines for Observational Studies, para 6.43)*
7. A legal opinion submitted with this application was given in relation to whether the research team could access the patient records, rather than whether the team could collect data prospectively without consent while the participants are patients.
8. Practically the distinction is arbitrary but should the Researchers redesign the protocol and resubmit the application with a set of dates in the past (e.g. 6 months), for which they are collecting information and be able to show that they cannot get consent for the reasons set out at para 6.43 above then the Committee could consider approving the study.

Decision

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

* The ethical standards for non-consensual studies that are stated in the Ethical Guidelines for Observational Studies are intended for application only to studies that are lawful.
* New Zealand law substantially limits the powers of health practitioners to do research without consent. It also substantially limits the powers of others to consent to participation in research on behalf of any person who is not competent. (See, the New Zealand Bill of Rights Act, 1990, the Protection of Personal and Property Rights Act 1988 and the Code of Rights, particularly Right 7(4).)

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| **8** | **Ethics ref:** | **19/STH/55** |
|  | Title: | The New Zealand National Stroke Registry |
|  | Principal Investigator: | A/Prof Annemarei Ranta |
|  | Sponsor: |  |
|  | Clock Start Date: | 28 February 2019 |

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

Potential conflicts of interest

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

Associate Professor Jean Hay-Smith declared a potential conflict of interest, and the Committee decided that it was not substantial and agreed that she could stay in the room for the discussion and decision-making in relation to this application.

Summary of study

The researchers wish to establish a national clinical registry of NZ patients (age 15 and over) who have a hospital discharge diagnosis of stroke (ischaemic or haemorrhagic). They wish to use data already collected during the clinical care of 20,000 patients. The purposes of the registry are to examine risk factors for, and outcomes of stroke. The researchers would also like to pool de-identified data from this registry with data from overseas registries.

Summary of resolved ethical issues

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

1. The key ethical issue for this project is the use of clinical data without individual consent. It appears that the researchers will only use retrospectively collected data, at least initially, for the purpose of clinical audit. Any proposal for future use of data for research would be submitted to the HDECs in separate applications for review.
2. As this project involves accessing health information without consent, the Committee noted that it can approve access to health information without consent if it considers the requirements set out at paragraph 6.43 of the *Ethical Guidelines for Observational studies* are met.

1) Obtaining individual consent would be impractical and may cause distress. This requirement is met with 20,000 participants, some of whom may now be deceased. Contacting all participants (or their relatives) would seem impractical and costly, and may cause distress to the relatives of those who have died from their stroke.

2) Obtaining individual consent would affect the scientific validity of the study. This is also met, as dead participants would be excluded and this would significantly bias any results

3) The benefit to public health outweighs the individual risks of being included in this study The risks to the individual are very low and the potential gains for public health are very high and the Committee considered this requirement was met.

Decision

This application was *approved* by consensus.

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| **9** | **Ethics ref:** | **19/STH/58** |
|  | Title: | Study Evaluating AZR-MD-001 in Patients with Meibomian Gland Dysfunction (MGD) and Evaporative Dry Eye Disease (DED) |
|  | Principal Investigator: | Dr Dean Corbett |
|  | Sponsor: | INC Research New Zealand Limited |
|  | Clock Start Date: | 28 February 2019 |

Mrs Naoko Chapman and Dr Dean Corbett were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of resolved ethical issues

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

1. Peer review submitted notes there have been four studies of topical ocular selenium use done in the 1950s and the Committee asked why so little research been done since then. The Researcher noted that it’s simply something that hasn’t been thought of in the intervening years.
2. Peer Review also indicates that stage 1 groups one and two are completed whereas the information sheet indicates that recruitment is currently open for all four groups. By the time the researchers come to recruit participants stage one and two will be fully enrolled.
3. Question b.4.4.1 in the application form: The Committee asked what the justification is for providing other researchers with data generated by the study in potentially identifiable form. This should not occur unless there is a compelling reason for it. The Researcher confirmed this was in error and any data generated by the study would be de-identified.
4. The response to question r.1.4 states there will be an independent DSMC, an internal DSMC and other data safety monitoring arrangements. The Committee asked which is correct. The Researcher advised that an independent data safety monitoring committee is in place, and that the company has its own internal DSMC.
5. Question p.3.1: The Committee advised that it prefers a small and well-identified group of people access medical records and asked which 'study staff' will be involved in accessing medical records, and who will make the first approach to potential participants. The researcher confirmed that no research staff will access the medical records and one-two clinicians will do this.

Summary of unresolved ethical issues

The main ethical issues considered by the Committee and that need addressing by the Researcher were as follows.

1. The Committee asked the Researcher what the risk to the participants is in relation to the requirement that they cease taking their usual treatments for either MGD or DED and that some will cease treatment to be randomised onto placebo. The Researcher explained that in participants with MGD there would only be risk if treatment is withheld for a long period of time and that won’t be the case in this study. Current treatments allow MGD to progress to its end stage. Investigators are anticipating that the study drug will have a more rapid and profound improvement. In other words, the course of the chronic disease will not progress for the same period of time. This will mean that the participants on placebo will have symptomatic but not-pathological changes that are unaddressed by the study medication. The Committee asked that the Researchers address in the information sheet the fact that participants’ symptoms may return and be problematic if they have to withdraw from treatment and are in the placebo arm.
2. The response to question p.1.1 states dry eye symptom questionnaires will be completed by participants; however a blank sheet of paper has been uploaded under 'surveys/questionnaires' in the documents section. Please clarify what is intended for the study. The Researcher advised that there is a standard form that will be given to participants. The Committee requested this document is uploaded when the researchers respond to this provisional approval decision.
3. The response to question r.2.3 states CRF will include subject code only. Please confirm that DOB will not be captured; as it usually is for demographic purposes.
4. The response to question r.3.7 states all samples will be labelled with participant code only. The Committee asked for clarification in relation to the following: whether this includes safety samples, what processes are in place to ensure potentially important clinical lab abnormalities are identified correctly when ID number is the only link to the participant, whether there is secondary checking of sample ID against volunteer by study staff, and whether safety samples will be retained until the end of the study as they are usually destroyed after 1 week.

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

1. The Committee noted the language is overly technical and in the interest of participants being able to make a fully informed decision about their participation in the study asked that the documents be revised and reworded in lay language.
2. The Committee queried the lack of a Māori tissue statement in the Participant Information Sheet. The Committee recommended the following statement: “*You may hold beliefs about a sacred and shared value of any tissue samples removed. The cultural issues associated with sending your samples overseas and/or storing your tissue should be discussed with your family/whanau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult prior to participation in research where this occurs. However, it is acknowledged that individuals have the right to choose.”*
3. The information in relation to pregnancy refers to contraception that is not available in New Zealand. The Committee asked that the information on reproductive risks provided in the HDEC template and available on its website be used instead: <https://ethics.health.govt.nz/guides-templates-forms-0/participant-information-sheet-templates>
4. PREGNANCY AUTHORISATION Please provide separate authorisation for collection of child's health information to be signed by a parent after the child is born.
5. p9. Please bullet point adverse events and give frequencies if available.
6. p9. Please add the risks associated with withdrawal of current treatment / exposure to placebo.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* paragraph6.22).
* Please provide a cover letter addressing the Committee’s outstanding concerns in relation to answers given in the application form.

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

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| **10** | **Ethics ref:** | **19/STH/59** |
|  | Title: | Delta |
|  | Principal Investigator: | Dr Dean Corbett |
|  | Sponsor: | Johnson & Johnson Surgical Vision |
|  | Clock Start Date: | 28 February 2019 |

Mrs Naoko Chapman and Dr Dean Corbett were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of study

1. This is an intraocular lens study in patients who will receive a lens replacement of some form. The study aims to assess usability of a pre-loaded disposable hand-held cartridge delivery system. This system comprises 2 parts: handpiece and cartridge. The Delta study will use the same cartridge as another approved study, the TITAN study, a pre-loaded intraocular lens.
2. A non-pre-loaded intraocular lens is the current standard delivery system made up of the lens, a cartridge and an injector used to inject the lens into the eye. The Researcher explained that the handpiece and cartridge will be investigated in this study – the cartridge is a pre-loaded intraocular lens loaded in the factory in a way that is reproducible and results in no change in rotation of the lens, less potential for marking in the lens and less potential for infectious contamination of the system because it is all a single piece. The Committee agreed that this explanation was much clearer than that given in the participant information sheets and asked the Researcher to revisit the information sheet and replace what is stated with similar wording.
3. The Committee’s general comment in relation to the participant information sheet is that it could be written in lay language so that the information is more accessible to participants.

Summary of ethical issues

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

1. The Committee noted that the Researchers had stated in the application form that this study raises no ethical issues. However, the Committee noted that some aspects of the delivery system will be used for the first time in humans in this study - the risks and the benefits are as yet unproven and this needs to be clearly stated to participants. Another ethical issue is that the researcher is also the patient’s clinician and there is potential for people to feel undue influence to be in the study. For future reference, these are the kinds of issues the Committee would like to see raised in the application to demonstrate that the researchers are alert to the ethical issues inherent in any study.
2. The surgeon’s experience will be the main outcome for the study. The Committee noted that the study also provides an opportunity to look at clinical outcomes such as lower risk of infections and shorter operation time. The Researcher explained that these outcomes are difficult to measure – infection is so rare that they would have to look at about 30, 000 cases before it is possible to measure that with any certainty, and in terms of shorter operation there is significant variability with the procedure and there is no time advantage in this particular study. The Committee noted that there is no control group in this study and the information recorded by surgeons in relation to operation time could be collected to compare it later with data from other studies.
3. The Committee queried whether the scoring system for the device in this study has been applied to other systems in the past and whether the threshold for acceptable performance of the system being 95% of responses above 3 (on 5 point scale) was valid. The Researcher noted that there is no benchmark and previous companies who have introduced preloaded systems to the research team have been introduced outside of the auspices of clinical trials.

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

1. Please review and rewrite the participant information sheet and consent form in lay language.
2. Please clearly state up front and in bold that this is a first-in-human study and that the risks and benefits are as yet unknown.
3. Only patients who have chosen a mono-focal lens will be included in this study. Page 2 of the PIS has information in it about multifocal lenses and the patient’s right to choose. The Committee asked that this information be removed as participants who have chosen a multi-focal option will not be invited to take part in the study.
4. The Committee noted that nurses and surgeons are going to complete the survey questionnaire as part of the study, and that the primary outcome will be to look at how the surgeon finds the device. The Committee asked the Researchers to consider including participant information sheets for the nurses and surgeons and noted that the patient participant information sheet in its current form reads as though it may have been written for clinicians.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* paragraph6.22).

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

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| **11** | **Ethics ref:** | **19/STH/60** |
|  | Title: | GA41024. A study of the trial asthma drug GDC-4379 in healthy participants and in adults with mild asthma. |
|  | Principal Investigator: | Dr Chris Wynne |
|  | Sponsor: | Roche Products (New Zealand) Limited |
|  | Clock Start Date: | 28 February 2019 |

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

Potential conflicts of interest

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

Dr Devonie Waaka declared a potential conflict of interest, and the Committee decided that she could remain in the room but not take part in the discussion or decision making for this application.

Summary of study

1. This is a first-in-human study of an inhaled drug for asthma. The study will be run sequentially in three parts in healthy volunteers and people with mild asthma: A) 32 healthy subjects given a single dose, B) 24 healthy subjects given doses over a 14 day period and, C) 12 mild asthmatics given doses over a 14 day period.

Summary of resolved ethical issues

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

1. The unknown risks of a new active substance (no previous clinical experience). However, the researchers have clearly informed participants of this on the participant information sheet with a boxed warning on page 1 that this is a first-in-human study.
2. The information sheet also includes information about the risks associated with similar medicines, although no frequencies have been given.
3. The Committee was pleased to see that the HDEC reproductive risks statements for men and women have been included.
4. The Committee noted that the dry powder inhaler used to deliver the new drug is a device and queried whether it is a standard dry powder inhaler similar to other devices already on the market or whether it is a novel device. The same device was used in another GDC drug trial that was done last year – it is just the drug that is new.
5. Part C of the study will be done by MRINZ and if they want to advertise then they will submit an advertisement for review as an amendment at a later stage.

Decision

This application was *approved* by consensus.

## Substantial amendments

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| **1** | **Ethics ref:** | **18/STH/240/AM01** |
|  | Title: | TARGET Protein Feasibility Study |
|  | Principal Investigator: | Dr Paul Young |
|  | Sponsor: | Prof Richard Beasley |
|  | Clock Start Date: | 01 February 2019 |

Dr Paul Young was present by teleconference for discussion of this amendment.

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 and addressed by the Researcher were as follows.

1. This amendment for a sub-study closely follows HDEC approval of the study and some content was part of the original protocol but not discussed as part of the original application in relation to the sub-study. The Committee asked the Researcher to explain what the decision process was for taking part in the nested sub-study and also why it is presented as a mandatory part of the main study when the protocol treats it as an optional sub-study for participants.
2. The Researcher explained that they have received grant money following approval of the study that enables them to set up the sub-study which was initially planned for one site in Australia. The mandatory requirement to take part in the sub-study in New Zealand was for reasons of simplicity. Introducing a separate consent process for doing an ultrasound and taking bloods out of existing lines would introduce complexity.
3. Information provided in the amendment and PIS/CF forms in relation to the time points that the blood will be taken: are the time points matched to when the ultrasound is being done or only taken at one time point? The Researcher confirmed no match to the ultrasound but that they would be taken on days the bloods are usually taken. The blood sample would be taken some time after the participant has left ICU. There are three sets of blood samples.
4. The Researcher explained that the literature suggests that muscle measurements are strongly associated with subsequent long term functional outcomes. Ultrasound findings will give the researchers additional clinical information about long-term functional outcomes. Excluding participants from a component of the study that is non-invasive and has no risk but improves the utility of the study overall is not in the best interests of participants given that they’ve already been enrolled in the main study having determined participation is in their best interests.
5. If someone doesn’t want to do the blood tests or the ultrasound they can withdraw their consent when competent. The Researcher confirmed that this notion extends beyond the study and participants can withdraw consent for any aspect of the study they choose. The Researchers would act in accordance with participants’ wishes. The Committee noted that the participant information sheet does not state that they have the option of having blood tests or ultrasounds done.
6. Blood samples will be batched and kept until the analyses are done at the end of the study. As soon as a patient recovers competence they can choose to have their blood used or not. This is not outlined in the information sheet as it stands. The Committee asked that this information be included in the information sheet as would any other aspect of the study – that participants have the option of having blood taken, used and stored.

Decision

This amendment was *approved* by consensus.

Non standard condition

Please include adequate information about the samples in the information sheet and consent form.

## 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:** | 09 April 2019, 12:00 PM |
| **Meeting venue:** | Sudima Hotel, Christchurch Airport, 550 Memorial Drive, Christchurch |

No members tendered apologies for this meeting

The meeting closed at 4.30pm.