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| **Committee:** | Central Health and Disability Ethics Committee |
| **Meeting date:** | 23 July 2019 |
| **Meeting venue:** | Room GC.3, Ground Floor, Ministry of Health, 133 Molesworth Street, Wellington |

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| **Time** | **Item of business** |
| 11:50am | Welcome |
| 11:55am | Confirmation of minutes of meeting of 25 June 2019 |
| 12:00pm | New applications (see over for details) |
| 12:00-12:25  12:55-1:20  1:20-1:45  1:45-2:10  2:10-2:35  2:35-3:00  3:00-3:25  3:25-3:50  3:50-4:15  4:15-4:40  4:40-5:05  5:05-5:30 | i 19/CEN/120  ii 19/CEN/124  iii 19/CEN/121  iv 19/CEN/125  v 19/CEN/118  vi 19/CEN/126  vii 19/CEN/116  viii 19/CEN/122  ix 19/CEN/123  x 19/CEN/115  xi 19/CEN/117  xii 19/CEN/113 |
| 5:30pm | General business:  Noting section of agenda |
| 5:45pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Mrs Helen Walker | Lay (consumer/community perspectives) | 01/07/2015 | 01/07/2018 | Present |
| Mrs Sandy Gill | Lay (consumer/community perspectives) | 30/07/2015 | 30/07/2018 | Present |
| Dr Patries Herst | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | Present |
| Dr Dean Quinn | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | Present |
| Dr Cordelia Thomas | Lay (the law) | 20/05/2017 | 20/05/2020 | Present |
| Dr Peter Gallagher | Non-lay (health/disability service provision) | 30/07/2015 | 30/07/2018 | Present |
| Ms Helen Davidson | Lay (ethical/moral reasoning) | 06/12/2018 | 06/12/2021 | Present |

## Welcome

The Chair opened the meeting at 11:50am and welcomed Committee members.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

## Confirmation of previous minutes

The minutes of the meeting of 25 June 2019 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **19/CEN/120** |
|  | Title: | AB-506-003: Safety, Tolerability, and Pharmacokinetics of AB-506 in Healthy Subjects for 28 Days |
|  | Principal Investigator: | Prof Ed Gane |
|  | Sponsor: | Novotech (New Zealand) Limited |
|  | Clock Start Date: | 11 July 2019 |

Prof Gane 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.

1. The Committee had no significant ethical concerns about this study and complimented the research team on a very well completed application.

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

1. Please remove Maori support contact details as this study will not involve Maori participants.

Decision

This application was *approved* by consensus.

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| **2** | **Ethics ref:** | **19/CEN/124** |
|  | Title: | ACHieve |
|  | Principal Investigator: | Prof Paul Hofman |
|  | Sponsor: | Pharmaceutical Solutions Limited |
|  | Clock Start Date: | 11 July 2019 |

Mr Gareth Corbett 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 Researcher introduced the study as a natural history study to gather information about growth patterns in a population of people who have Achondroplasia. The research team will also gather information on presenting co-morbidities in this population to provide background information; the study’s global sponsor has a potential treating compound that it may use in future trials in this population.

Summary of resolved ethical issues

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

1. The Committee queried whether the researcher has any known statistics about the prevalence rate of dwarfism in Māori. The researcher noted that he is not aware of any particular statistical differences or increases or decreases in prevalence rates for Māori. For future reference the Committee noted that the answer at question p.4.1 on the application form should include any known statistics about the condition in Maori and how the study outcomes might benefit Māori.
2. The peer review submitted with this application is from the study sponsor. The Committee noted that it expects to see peer review of a study protocol from someone who is independent of the study and has the expertise to provide comment. The HDEC has a template you can find on its website <https://ethics.health.govt.nz/guides-templates-forms-0/scientific-peer-review-submissions-%E2%80%93-guidance> that could be completed by an independent reviewer and submitted to the Committee The Researcher will go back to the sponsor and talk with the company about seeking review of a paediatrician independent of this study.

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

PIS/CF for children

1. The Committee noted that the language is directive and asked that the researchers review the document with this in mind. For example, “You will have to follow the instructions that your parents/guardians/doctor give you.” could be reworded along the lines of “You’ll be asked to follow instructions about the study…”.
2. Another example on page 3 of 6: “If you decide not to be in the study or change your mind no one will be angry with you and you will not upset anyone.” The Committee noted that the research team can’t guarantee that parents won’t be grumpy with the child and suggested expressing this differently along the lines of “Changing your mind won’t upset us and we won’t be grumpy”.
3. The Committee suggested that participants in this age group could benefit from an information sheet that has simplified wording and includes more pictures.
4. The Committee noted that referring to Achondroplasia as a “sickness” under the heading ‘Will being in the study help me?’ could be seen as stigmatising and suggested that this could be rephrased to say something like “people who look like you”.
5. Please include contact details for the study’s Maori support person in the child assent form.

PIS/CF for parents/guardians

1. Data from this study will go to the sponsor overseas. While this is stated in the information sheet it is currently not stated on the consent form and the Committee requested a statement to this effect be included on the consent form.
2. Some of the language included is technical anatomical language e.g Foramen Magnum size and index values. The Committee asked the researchers to simplify and explain what these terms mean.
3. Page 4 of 13 notes that the researchers are going to inform participants’ general practitioners that they are taking part in this study. The researcher explained that the reason for this is that participants will be seeing another medical practitioner and it would be beneficial for their general practitioners to know of their participation.
4. The Committee asked why participants will be able to receive medications that are considered necessary by the investigator. The researcher explained that they are just observing them and could change this to read “medications that are considered necessary by your doctor”.
5. The consent form states that assent is required for children 7 or 8 years old and the Committee asked why only these ages are mentioned when any child can refuse to take part. The researcher noted that for ages 6 years and under they will talk to the children who will give assent and have this documented by the investigator. The Committee asked that the statement be reworded to note that all children are asked to assent but only 7 and 8 year olds will be given a form to sign. The Committee asked the researcher to add that if any child dissents then they won’t be asked to proceed. In other words, any child can say ‘no’ to taking part in the study.
6. Page 3 of 13: the Committee noted that certain information is taken during the enrolment and screening visits including the age they were diagnosed and foramen magnum size from their medical records and asked whether collection of this information needs to be repeated at every visit. The researcher confirmed they’d only need to collect from the medical records and there wouldn’t be a need to repeat the questions at each visit.

Decision

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

* Please provide evidence of favourable independent peer review of the study protocol (*Ethical Guidelines for Intervention Studies* Appendix 1).
* Please amend the information sheet and consent forms, taking into account the suggestions made by the committee *(Ethical Guidelines for Observational Studies* paragraph *6.10)*

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

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| **3** | **Ethics ref:** | **19/CEN/121** |
|  | Title: | Cemiplimab Treatment After Surgery and Radiation Therapy in Patients with High Risk Cutaneous Squamous Cell Carcinoma |
|  | Principal Investigator: | Dr Andrew Macann |
|  | Sponsor: | Regeneron Pharmaceuticals Inc |
|  | Clock Start Date: | 11 July 2019 |

Ms Sophie Corbett 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.

1. The Committee congratulated the research team on a well-completed application noting that this study is an interesting one which the Committee understands will involve adding an extra antibody after surgery and radiation in patients with high-risk cutaneous squamous cell carcinomas. The research team intend to enrol eight patients in New Zealand. An application has been submitted in parallel to SCOTT.
2. The Committee had no significant ethical concerns in relation to this application but noted a few changes that it would recommend be made to the participant information sheets and consent forms.
3. The Committee noted, for future reference, the application form question f.1.2 asks about other ethnicities and any known prevalence rates. If there are no known prevalence rates across other ethnicities then it is helpful to state this.

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

Main PIS/CF

1. Page 5: please revise for differing font sizes.
2. Page 18 mentions various regulatory bodies that will have access to information as well as “other” regulatory bodies from other countries. The Committee asked that the other regulatory bodies be specifically stated. i.e. MedSafe and New Zealand HDECs.
3. The Committee noted submission of the following participant information sheets and consent forms: Part 1, Part 2, Optional Genomics sub study, Future Unspecified Research and Pregnant partner. The Committee queried whether the main information sheet has adequate provision is made for the pregnant participant. It noted there is mention about the importance of not getting pregnant and, that there will be follow up (with participant permission), should someone become pregnant while on the study. In contrast, partners who may become pregnant are given a separate information sheet and other consent forms including follow up and the Committee suggested that the main information sheet and consent form could include another bullet point that specifically states that they agree, should they become pregnant, that they are happy to be followed up. The Researcher agreed that they could include this information.
4. Please include the recommended compensation statement and the pregnancy statement from the HDEC PIS/CF template that you can find on the HDEC website at: <https://ethics.health.govt.nz/guides-templates-forms-0>. The template lists the contraception methods that are acceptable and highly effective and this is helpful information for participants to make a decision on.
5. CT scan section includes a statement about radiation exposure compares it to one year’s natural background exposure. It then goes on to say no one knows for sure whether exposure to low amounts of radiation is harmful for your body and, that scientists believe that being exposed to too much radiation can cause too harmful side effects. The Committee queried the factual accuracy of these statements and recommended that these statements be deleted as they don’t add helpful information.

Part 1 PIS/CF

1. After the bullet points on page 13 there is a statement that reads “As of March 2018 in all patients treated in all studies there were 8 deaths”. The Committee noted that it could be helpful for potential participants to know many people there have been in the other studies to put the number into context. For example 8 out of 10 participants or 10,000 participants.

Part 2 PIS/CF

1. The Committee noted that this is the information sheet for participants who relapse. The information here suggests that the same number of participants will be in part 2 and queried whether they expect that all patients will relapse? The Researcher explained that they don’t expect this and the reason for including this number was to cover the worst case scenario but in fact the possibility of relapse is lower and they could talk to the sponsor about making this information more accurate. The Committee suggested that the information sheet could state that this part of the study is open to all who were involved in the first part of the study and who have relapsed.
2. In relation to the risks involved in taking part in this study there are a few sections that state same risks apply as in Part 1. The Committee noted that there could be a time lag between the two parts of the study and in the interest of making information easily available to people the Committee queried whether participants will have Part 1 readily available to refer to. The Committee recommended that either participants either have the Part 1 form made readily available to them or have some information repeated in Part 2 so that information is accessible at the time rather than having to go back to previous forms.

Optional Genomics sub-study PIS/CF

1. The heading on the Consent form needs to clearly relate to this optional study so that it is clear that this sits with the optional genomics sub-study. The same applies for the future unspecified research participant consent form. Please clearly state on both headings.
2. Please include a statement that data is going overseas on the following consent forms: Optional Genomic sub-study, Future Unspecified Research and Pregnant Partner.

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* paragraph *6.22*).

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

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| **4** | **Ethics ref:** | **19/CEN/125 – CLOSED MEETING** |
|  | Title: | Phase 3 study of SBRT ± pembrolizumab for participants with medically inoperable Stage I or IIA NSCLC |
|  | Principal Investigator: | Dr Gareth Rivalland |
|  | Sponsor: | Merck Sharp & Dohme (Australia) Pty Limited |
|  | Clock Start Date: | 11 July 2019 |

Dr Gareth Rivalland and Mrs Pallavi Wyawhahare 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.

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* paragraph *6.22*).

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

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| **5** | **Ethics ref:** | **19/CEN/118** |
|  | Title: | Pilot study for determining the prevalence of drug use in trauma patients in the Emergency Department |
|  | Principal Investigator: | Professor Ian D Civil |
|  | Sponsor: |  |
|  | Clock Start Date: | 11 July 2019 |

Prof Ian Civil and Ms Siobhan Isles were present in person 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 this study

1. When people come into hospital in the situation of a trauma call, they go through a standardised process that includes having a range of bloods taken with a single draw that is used for a range of tests. The proposal in this version of the protocol is that there is an additional sample taken for the secondary purpose of this research. The previous protocol proposed use of left over routinely collected sample at the lab but the Researchers were concerned that increased the risk of an individual being identified as samples are labelled. The idea with this protocol is that the sample would be placed in a tube without any patient identifiers before being sent to the lab.
2. The reason for this prevalence study is that nothing is known about the prevalence of the illicit substances in traumatic events as the police sampling process and existing hospital sampling process is selective and does not test for the types of drugs or levels apart from the fact that someone may have had some exposure to an illicit substance.
3. Patients will not be competent to consent at the time that this additional sample is taken for the intended use in this research.

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 noted the HDC Patient Code of Rights Right 7(4) which says that where a consumer is not competent to make an informed choice, no person is there to consent on their behalf then the provider may provide services where it is in the “best interests” of the consumer. The Researchers have argued that the intended study is in the best interests of the consumer as it is good for society. Running that argument with Prof Green’s research in the ‘unfortunate experiment’ had he been right and had those interventions not been necessary, to discover that would have benefited society and therefore have been justified. The Code is a response to the unfortunate experiment and informed consent is the keystone of the Code. If people can’t consent then Right 7(4) needs to be met. The Committee noted that if the Research team wants to conduct this study then it would need to get legal advice about whether the study meets the best interests of the consumer test. Right 7(4) test is not about whether there is a risk or burden to the consumer, it is about whether they would be better off by being in this research than they would have been had they not been in the research. The Committee is not able to approve an application if it does not meet the legal test.
2. The Researchers noted that this process denies them the knowledge that may, in time, allow them to treat a significant issue for society with the urgent attention it needs. The Committee acknowledged the value of the intended research and noted that should the protocol allow for an arrangement where there is use of left over sample taken from routinely collected blood then the Committee could consider the application in accordance with Right 7(10)(b) of the Code and might ethically approve the study. The Committee would still need to consider the ethical issue of enrolling people in a study and not telling them if it were to consider approving the unconsented secondary use of tissue taken as part of a health care procedure under Right 7(10)(b).
3. The Researchers noted that they had looked in-depth with other clinicians into how they might use the left-over samples without identifying the individual but this could be challenging. Even at a big hospital the number of samples sent to ESR are low (one or two a day), and these tests are rarely done by ESR outside of the criminal process.
4. The Committee suggested that the Researchers get legal advice about whether they could run an argument that Right 7(10) (b) applies in the case of obtaining blood in the course of a health care procedure and using left over samples for this research. With any legal advice submitted the Committee would also want to consider and weigh up the issue of not disclosing to patients, when they are conscious, that some of their routinely collected blood had also been tested for research purposes.

Decision

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

* HDECs can approve an application when they are satisfied that intended research is both ethical and is consistent with New Zealand law. The Committee suggested that the Research team seek legal advice about whether an argument can be made that Right 7(10)(b) of the Code of Rights applies in the case of obtaining blood in the course of a health care procedure and using left over samples for this research.
* The research team may also wish to consider rewriting the study protocol to make clear that the use of tissue will be for left over samples from blood routinely taken as part of a standard health care procedure.

This information will be reviewed, and a final decision made on the application, by full committee by teleconference.

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| **6** | **Ethics ref:** | **19/CEN/126** |
|  | Title: | Ketamine in anorexia nervosa |
|  | Principal Investigator: | Prof Paul Glue |
|  | Sponsor: | Novotech (New Zealand) Limited |
|  | Clock Start Date: | 11 July 2019 |

Prof Glue 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.

Dr Cordelia Thomas declared a potential conflict of interest, and the Committee decided that it was not significant and that she could remain in the room for the discussion and decision-making for this application.

Summary of resolved ethical issues

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

1. The Committee thanked Prof Glue for the reapplication and noted that the letter of response had addressed the points raised in the original review well. The protocol has been amended and the researchers will just look at the pharmacological response and the lower BMI range has been amended from 13 to 15.
2. The application form stated that the Researcher will notify participants *and their families* of any improvements and the Committee queried under what authority family would be notified. The committee noted that there was no provision in the consent form for the participant to consent to this. The Researcher noted that this may be an oversight and, that as they will enrol only those able to give consent, that there is no necessity to notify families.

Summary of outstanding ethical issues

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

1. The Committee asked Prof Glue to clarify whether or not this is a pilot study. Prof Glue explained that they are looking at relatively small numbers of people. Dose is still poorly understood even with two published case series so there is an exploratory component to the study and Prof Glue would therefore express this as a pilot study. The Committee noted that this is a pilot study does not come across clearly in the participant information sheet and, from the peer reviews submitted that it is an early entry part of the research as well as whether or not this research is particularly mainstream.
2. One of the Committee’s concerns was that the question the previous Committee posed about the peer reviews. Four peer reviews were submitted with this application and they were either incomplete, unsigned or undated and they were completed in 2018 and seemed to pertain to a previous version of the protocol. The Committee noted that it is not expert on the pharmacodynamics and kinetics of Ketamine nor on psychiatry or psychology and therefore what it needs to see is at least one independent peer review that is based on the current protocol.
3. Prof Glue noted that getting someone who is expert in eating disorders and interested in exploratory clinical pharmacological studies and understands Ketamine could be challenging as there are few people with those particular skill sets. Sue Luty who was one of the original reviewers could be well placed to review. The Committee noted that Prof Glue could give Sue Luty the HDEC peer review template and ask her to add comments to show that review has been thorough. The Committee likes to see the process whereby there has been a thorough review and feedback and, incorporation of any suggestions in the protocol. The Committee noted it appreciates that the research is in a specialised area and may be outside of normal considerations of treatment for anorexia nervosa which is enduring, but given the make-up of the Committee and its role peer review is important as the Committee does not have the scientific expertise to assess the protocol and these peer reviews form an important part of the process.
4. The Committee noted the information sheet states that the researchers are looking at potentially providing people with post-study Ketamine for a further three months. The Committee noted it would find it helpful to get some feedback about why this is being considered and why three months is being considered. The Committee couldn’t perceive much empirical evidence behind why this extension part is considered and if the Researcher is going to consider it would be good to have it as part of the study but formalised into the study rather than simply providing it to people.
5. Prof Glue explained that what they have found with Ketamine is that about two-thirds to three-quarters of people with severe depression or anxiety or obsessionality will show an improvement within an hour or so of dosing. Typically, within 3-7 days the effects wear off. Rather than have people with anorexia who have those mood symptoms get better for a few days and then the effects wear off there is a recently published paper in patients with treatment resistant anxiety who were treated for three months. This is the first paper published on maintenance treatment for any condition treated with Ketamine and the Researchers found that for a majority of patients they could keep them in a well state over the three months and a quarter of people didn’t show any relapse after stopping treatment. Prof Glue can include this information as it provides a rationale for doing maintenance and, an idea of what the potential outcomes might be like.
6. The Committee noted it would be more reassured if this is incorporated as part of the actual study, as they are ostensibly prescribing off-label, rather than within the framework of a clinical trial. Prof Glue explained that a condition of going into the maintenance trial is that they show 50% improvement on one of the rating scales, whether that is anxiety or depression. This would mean that people who weren’t showing any improvement weren’t then getting exposed to the drug for a subsequent three months.
7. The Committee clarified with Prof Glue that this three months of treatment will be part of a maintenance study. Prof Glue confirmed this and explained that if people show a measure of improvement as 50% greater in depression or anxiety ratings they are then eligible to go into maintenance treatment and the rationale behind that is that even if people do show a response, the effects only last for up to a week. The Committee asked that this be made much clearer in the information sheet as the information sheet as it stands presents more like off label prescribing rather than maintenance.

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

1. The Committee asked that the following information stated in the application form for this study be included in the participant information sheet: the screening tests that will be done, that the participant will be asked for their health information from the medical or psych team at the screening test, that blood and urine will be collected and tissue collected for safety assessment, when the study might be terminated and what happens around those circumstances. The Committee asked the Researcher to check that all relevant information is transferred across to the information sheet as it is important information for the participant to know.
2. Page 1 of 8 talks positively about Ketamine improving symptoms of depression rapidly. The Committee understands that improvements largely are short-lived and asked that the Researchers make this clearer as the wording as it stands suggests Ketamine is a cure.
3. Page 2 of 8 states that two groups from the UK reported that and the average participant won’t know that this is in relation to research projects and findings. The Committee asked that the “two groups” be made clearer.
4. Page 2 of 8 under the heading ‘What will my participation in this study involve?’ The sentence “Because the medications are given orally we do not think you will notice side effects from any of these doses.” may be misleading as it suggests that there are no possible side-effects from Ketamine when there are and they are detailed on later pages in the information sheet. The Researcher explained that the oral dosing is strikingly different in terms of the side-effect profile and when the drug is given by injection it is clear within five minutes that the drug has been administered. Because the oral dosing (at rates of dosing for this study), has a much slower rate of entry into the body the peak concentrations are lower and the side-effect profile is different and the Researcher expects that people won’t report side-effects. The Committee asked that the Researcher give more context to the above-mentioned statement.
5. Page 5 of 8 talks about seeking consent from a pregnant partner giving consent for her and her infant’s information being collected. The Committee queried whether it is the intention to follow up a pregnant partner and birth of her child? The Researcher noted that participants won’t be menstruating (as it is one of the side effects of the illness in this population), and they tend not to be sexually active. In practical terms it is unlikely that the Research team will see a pregnancy in this study. The illness is uncommon in males and generally in this well-established population it is almost entirely young women. Even if a pregnancy will be unlikely, the Committee noted that the statement should remain. An additional information sheet is needed for the pregnant partner or participant and, if the Research team want to collect information about the child after birth provision for a guardian to consent on behalf of the child after the birth is needed.
6. Page 6 of 8 has the statement that data will be securely stored and also states when it will be destroyed. The Committee asked that the Researcher reference here the participant rights under New Zealand privacy legislation to request access to and correction of their health information. The Researcher can reference the HDEC participant information sheet and consent form template for guidance on the statements to use: <https://ethics.health.govt.nz> The Committee asked that the Researcher also replace the current compensation statement with the statement from this template.
7. Page 6 of 8 also states if participants want to access personal data later they will need to record the identification number used for their particular test and the Committee asked the Researcher to clarify this statement. The Researcher explained that all who enter the study are given a number and all of the information stored under the participant number and agreed to expand on the statement so that participants know what the number refers to. The Committee noted that it would usually expect to see an explanation that the samples will be de-identified and given a code and, how they will be used throughout the process.
8. The consent Form seeks consent for the participant’s GP or provider to be informed about their participation. The Committee asked that this information be included in the information sheet so that participants aren’t reading it for the first time in the consent form.
9. The Committee queried what will happen in cases where participants don’t improve who then aren’t followed up because they are not in the three month maintenance programme. The Committee was concerned that they may feel despair that their symptoms haven’t improved and queried what safety mechanisms are in place for this group of participants. The Researcher noted that the people he is treating have not improved on any other treatment options and in many cases there are no further options but they would usually continue to be cared for by their GP or community mental health team with standard case management. If participants don’t show an improvement in mood during the dose ranging part of this study they will return to standard of care. Managing distress in the acute unit is part of the Researcher’s clinical role and he noted in terms of what can be done in a research environment if participants haven’t shown a response to the intervention this is to get into a clinical management role. His worry is that this could be seen to blur the line between research and clinical practice.
10. The Committee noted that the Researcher notes in the application form that the head is seen as Tapu for Māori. The Committee noted that taking tissue is also considered Taonga and asked that the Researchers include the following statement in the information sheet as well as noting the Tapu of the head given that they are asking permission to put a cap on participants.

“*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.”*

Decision

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

* Please provide evidence of favourable independent peer review of the study protocol (*Ethical Guidelines for Intervention Studies* Appendix 1).
* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* paragraph *6.22*).

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

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| **7** | **Ethics ref:** | **19/CEN/116** |
|  | Title: | Eidos AG10-301: A study to measure how effective and safe AG10 is for the treatment of Symptomatic Transthyretin Amyloid Cardiomyopathy |
|  | Principal Investigator: | Dr Hugh Goodman |
|  | Sponsor: | Pharmaceutical Research Associates New Zealand Ltd |
|  | Clock Start Date: | 11 July 2019 |

Dr Hugh Goodman 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.

1. The Committee queried how long the open label extension would go on for. The Researcher stated the sponsor indicated that participants would remain on it for as long as it benefitted them.

Summary of outstanding ethical issues

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

1. The Committee noted the application stated health information would be stored for 15 years whereas the PIS stated 10 years. The Committee advised that either will be acceptable and requested the Researcher correct this for consistency.
2. The Committee advised that for future applications it would be helpful to include any statistics or data regarding the prevalence of the disease in Māori for question P.4.1. The Committee advised that if this was unknown to please state so as this information is useful to the Committee. The Researcher stated they had not personally observed the hereditary form of the condition in a Māori patient and ethnic prevalence data on the non-hereditary type was currently unknown.
3. The Committee noted the insurance was due to expire in January 2020. The Researcher confirmed this would be renewed.

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

1. The Committee commended the Researcher on a well written PIS. The Committee requested the inclusion of a table of visits and procedures (illustrating a schedule of days, doses etc.).
2. The Committee queried whether in the event of a pregnant participant / partner the Researchers intended to follow information on the baby. The Researcher stated they believed they would want to know the outcome of the pregnancy and any health or developmental issues of the baby. The Committee advised that a separate consent would need to be obtained after the birth. The Committee requested an additional bullet point on page 20 of the main PIS to explain this.
3. The Committee queried the reference to a participant’s ‘primary doctor’ on page 16 of the main PIS and whether this referred to their GP. The Researcher stated it did and agreed to amend it.
4. The Committee requested the “Who do I contact for more information?” section on page 13 be moved to the end of the sheet for easier accessibility.
5. The Committee requested the addition of a laypersons explanation of technical terms (e.g. double-blind treatment, open label extension) discussed in the PIS on page 2.
6. The Committee requested long paragraphs (for example the 2nd paragraph on page 3 and 2nd paragraph on page 12 in the PIS) be split into bullet points.
7. The Committee suggested including the phrase “see below” when discussing procedures and tests as these are explained later in the PIS.
8. The Committee requested the Researcher change the word ‘volunteer’ to ‘participant’ on page 8. The Committee suggested revising the statement to just say “provide consent”.
9. The Committee noted an inconsistency in section 14 stating that participants can change their mind and have their samples destroyed but the next page states that if allowed by law the samples may be retained and used. The Committee requested the second statement be removed as every participant has the right to withdraw their consent.
10. The Committee requested the inclusion of a cultural statement (available from the HDEC template) when discussing sending tissue overseas on both the main PIS and pregnant partner PIS.

Decision

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

* Please submit an updated Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee. (*Ethical Guidelines for Intervention Studies* paragraph *6.22*).

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

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| **8** | **Ethics ref:** | **19/CEN/122** |
|  | Title: | A Randomized, Multicenter, Double-blind, Parallel, Active-control Study of the Effects of Sparsentan, a Dual Endothelin Receptor and Angiotensin Receptor Blocker, on Renal Outcomes in Patients with Pr |
|  | Principal Investigator: | Dr Kannaiyan Rabindranath |
|  | Sponsor: | IQVIA RDS Pty. Limited |
|  | Clock Start Date: | 11 July 2019 |

Dr Kannaiyan Rabindranath was not 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 need addressing by the Researcher were as follows.

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

1. The Committee queried whether the intervention was a combination drug.
2. The Committee advised that if the Researchers intended to collect any health information on a pregnant participant / partner’s baby after the birth this would require a separate consent process. The Committee requested the PIS be amended to include this.
3. The Committee noted that blood samples banked for not yet known research purposes fell under Future Unspecified Research. The Committee requested a separate consent form for this. The Committee advised that ta template for this is available on the HDEC website.
4. The Committee requested an overall revision of the PIS to include explanations of medical terminology and make it more layperson friendly.
5. The Committee noted that the New Zealand arm would not include child participants and requested any references to children removed from the PIS.
6. The Committee advised that for future applications when answering question P.4.1. it would be helpful to include information on the prevalence of the disease in Māori supported by statistics and whether the research may benefit Māori rather than an inappropriate reference to Article 1 of the Treaty of Waitangi
7. The Committee recommended including clear information for each ‘phase’ of the study. The Committee suggested a flow diagram demonstrating screening, treatment, follow up may be useful.
8. The Committee requested the inclusion of Māori health contact information in the PIS.
9. The Committee requested the inclusion of information regarding sending data overseas in the pregnant participant / partner form.
10. The Committee noted inconsistent formatting (font size, spaces etc) in the PIS and requested a thorough proof-read.
11. The Committee requested clarification to the unblinding section as this was potentially difficult to understand.
12. The Committee requested references to ‘your race’ and grouping results by race are removed as this is not appropriate for a New Zealand context.
13. The Committee advised that participants should not be responsible for informing the GP and if they consent to it the onus is on the study team to make the notification.
14. The Committee requested the statement instructing participants not to take their study medication on days they visit the doctor be bolded for emphasis.
15. The Committee advised that proxy consent was inconsistent with New Zealand law and requested any mention of legal guardians of adults be removed
16. The Committee requested a statement informing participants that HIV is a notifiable disease.

Decision

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

* Please amend the Participant Information Sheet and Consent Form, taking into account suggestions made by the Committee. (*Ethical Guidelines for Intervention Studies* paragraph *6.22*).
* Please supply an optional form for Future Unspecified Research. (*Ethical Guidelines for Intervention Studies* paragraph *6.22*).

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

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| **9** | **Ethics ref:** | **19/CEN/123** |
|  | Title: | (duplicate) CA045-001 |
|  | Principal Investigator: | Dr Catherine Barrow |
|  | Sponsor: | Bristol Myers Squibb |
|  | Clock Start Date: | 11 July 2019 |

Ms Maureen Blakemore 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.

1. The Committee noted this was a re-submission of a previously declined application with a large number of points and thanked the Researcher for their detailed response.
2. The Committee queried whether the drug has been submitted to SCOTT. The Researcher confirmed it had.
3. The Committee noted the application suggested a radiation safety report would be obtained and queried whether this had been undertaken. The Researcher stated it had not and this was left in error.
4. The Committee noted an option in the consent form about including or excluding genetic information. The Committee advised that if an option was to be made on the consent form then it would need information to fully explain it in the main PIS.
5. The Committee queried the reimbursement to be made through Greenphire and whether participants could withdraw their information from this third party. The Researcher stated it was their understanding that they could. The Researcher stated if participants were not comfortable with a third party having their data they could not opt-in and could receive their reimbursement through standard means. The Committee requested information explaining this be added to the PIS.
6. The Committee advised that as the age of consent is 16 the assent form should be changed to 12 – 15. Any competent participants 16 years or older can consent as adults.
7. The Committee queried the basis for including 12 – 15 year olds in the study. The Researcher stated it was an opportunity to include this particular age group which is often overlooked. The Researcher stated many trials exclude participants younger than 16 and the DHB is trying to be more inclusive. The Researcher stated though it was uncommon there were some individuals under 16 years old with melanoma and they are frequently ineligible to receive access to both trials and funded therapies due to their age. The Committee advised that the benefits of access to an experimental drug would have to be weighed against its risks. The Researcher stated that as this was a phase 3 trial they know there is efficacy. The Researcher stated every individual participant would have the potential benefits and potential risks explained during the informed consent process. The Researcher stated that access to the drug is crucial for any younger participants as life expectancy with melanoma can be as little as 6 – 12 months.
8. The Committee queried whether the study had a safety protocol for if a participant indicated severe distress or suicidal ideation. The Researcher stated they would refer them as appropriate. The Committee requested confirmation on whether there was an ‘electronic threshold’ for notifying the site to any online responses indicating distress.
9. The Committee queried whether the Researcher knew of the prevalence of melanoma in Māori. The Researcher stated it was not as common in the Māori population but they were seeing an increase as more people identify as Māori. The Committee advised that this information is useful to include in future applications rather than inappropriately citing the Treaty of Waitangi.

Summary of outstanding ethical issues

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

1. The Committee noted the assent form was still dense and queried whether the Researcher believed an average 12 year old could properly comprehend it. The Researcher stated they have tried to address this and would create an environment to ensure they had appropriate time to absorb the information and ask questions. The Committee suggested that assent forms usually have more white space, more pictures, simpler language and less intimidating paragraphs and recommended the Researcher try to make it as age appropriate as possible.
2. The Committee advised that there is a legal distinction between a child’s legal guardian and an individual having the child ‘in their care’. The Committee advised that only the legal guardian is entitled to consent on behalf of the child. The Committee requested the removal of any references to a child “in your care” be removed as this proxy consent is inconsistent with New Zealand law.
3. The Committee noted information in the main PIS about mandatory consent for biomarkers on page 27. The Committee queried whether FUR was mandatory as the FUR consent form stated it was optional. The Researcher stated this would as error and confirmed the FUR was optional. The Committee requested the information be removed from the main PIS.

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

1. The Committee requested the addition of identifiers to the consent form as it was not currently clear what each form was for (e.g.FUR or Greenphire etc).
2. The Committee requested additional information on the optional FUR PIS to explain its purpose, follow-up testing, uses of information and data privacy policy, risks etc.
3. The Committee advised that there may be a long period between signing and agreeing to the study and treatment beyond progression and requested the information either be repeated or a copy of the main PIS be attached.
4. The Committee queried in what scenario it may be possible that a unique identifier is unable to be used for participant data being sent to the sponsor (page 29 of the parent/guardian PIS). The Researcher stated they could not think of one and believed the sponsor was covering itself. The Researcher confirmed only study ID number and year of birth are sent.
5. The Committee requested information explaining who would have access to participant data and for what purpose (e.g. data monitors) be added to all information sheets.
6. The Committee requested an overall revision of each PIS to check for consistency and grammar.

Decision

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

* Please amend the Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* paragraph *6.22*).
* Please submit a safety protocol. (*Ethical Guidelines for Intervention Studies* paragraph *5.39*).
* Please submit an optional form for Future Unspecified Research. (*Ethical Guidelines for Intervention Studies* paragraph *6.22*).

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

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| **10** | **Ethics ref:** | **19/CEN/115** |
|  | Title: | Phase 3 Study of Pembrolizumab with or without Maintenance Olaparib in First-line Metastatic Squamous NSCLC |
|  | Principal Investigator: | Mr Brendan Luey |
|  | Sponsor: | Merck Sharp & Dohme (Australia) Pty Limited |
|  | Clock Start Date: | 11 July 2019 |

Mr Brendan Luey and Ms Maureen Blakemore 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. The Committee queried the status of pembrolizumab in New Zealand for this type of cancer. The Researcher stated it was registered for non-small cell lung cancer but not funded. The Committee requested the statement indicating it ‘may not’ be approved be clarified.
2. The Committee queried what would happen in the event a participant became pregnant and would the study team follow them. The Researcher stated it would be very bad as these are terminal patients taking a cytotoxic drug. The Researcher stated most participants would be beyond child bearing age. The Committee accepted that if it was extremely unlikely that a participant would become pregnant then a pregnant participant PISCF would not be needed.
3. The Committee queried whether a submission had been made to SCOTT. The Researcher confirmed it had.
4. The Committee queried the answer to question R.1.3. in the application about radiation exposure and whether participants would receive CT scans. The Researcher stated they may get one or two additional scans but most are part of standard care for people having this treatment.
5. The Committee advised that for future applications when answering question P.4.1. it would be helpful to include information on the prevalence of the disease in Māori supported by statistics and whether the research may benefit Māori rather than an inappropriate reference to the Treaty of Waitangi
6. The Committee queried how potential participants would be identified. The Researcher stated they have a single cancer centre in the region that all patients with lung cancer are referred to for chemotherapy. The Researcher stated if any patients were eligible they would have the study discussed with them at clinic.

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

1. The Committee queried an item on the PIS about receiving a lay summary ‘unless notified’ by a doctor. The Researcher stated the intention was an option for a participant’s doctor to explain the results to them rather than an article. The Researcher stated this would be removed.
2. The Committee requested information explaining the questionnaires be added to the PIS as it does not currently include this under the “What do I do on my own?” section on page 5.
3. The Committee noted this was a very involved study and recommended including a flow diagram on the PIS to illustrate what is different to standard care and what changes participants will have by being part of the trial. The Committee stated it could be a simple demonstration of screening to induction to maintenance splitting off into different branches.
4. The Committee requested the statement on page 4 of the PIS that HIV and hepatitis MAY be reported be changed to MUST be reported as these are notifiable diseases.
5. The Committee advised that there was no consent on the consent form for samples to be sent overseas. The Committee requested a point adding this be included.
6. The Committee queried a statement on page 11 of the PIS discussing tumour tissue samples sent overseas and noted another reference in the application about blood going overseas. The Committee requested clarification as to what would be sent overseas. The Researcher stated they believe any blood and urine samples would be tested at the local laboratory and would revise the paragraph for clarity.
7. The Committee requested the Researcher ensure that it is clear in the PIS that participants have the right to request and correct information held about them in the study.

Decision

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

* Please amend the Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee. (*Ethical Guidelines for Intervention Studies* paragraph *6.22*).

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

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| **11** | **Ethics ref:** | **19/CEN/117** |
|  | Title: | Phase 3 Study of Pembrolizumab with Maintenance Olaparib or MaintenancePemetrexed in 1L Metastatic Nonsquamous NSCLC |
|  | Principal Investigator: | Mr Brendan Luey |
|  | Sponsor: | Merck Sharp & Dohme (Australia) Pty Limited |
|  | Clock Start Date: | 11 July 2019 |

Mr Brendan Luey and Ms Maureen Blakemore 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. The Committee queried the status of pembrolizumab in New Zealand for this type of cancer. The Researcher stated it was registered for non-small cell lung cancer but not funded. The Committee requested the statement indicating it ‘may not’ be approved be clarified.
2. The Committee queried what would happen in the event a participant became pregnant and would the study team follow them. The Researcher stated it would be very bad as these are terminal patients taking a cytotoxic drug. The Researcher stated most participants would be beyond child bearing age. The Committee accepted that if it was extremely unlikely that a participant would become pregnant then a pregnant participant PISCF would not be needed.
3. The Committee queried whether a submission had been made to SCOTT. The Researcher confirmed it had.
4. The Committee queried the answer to question R.1.3. in the application about radiation exposure and whether participants would receive CT scans. The Researcher stated they may get one or two additional scans but most are part of standard care for people having this treatment.
5. The Committee advised that for future applications when answering question P.4.1. it would be helpful to include information on the prevalence of the disease in Māori supported by statistics and whether the research may benefit Māori rather than an inappropriate reference to the Treaty of Waitangi
6. The Committee queried how potential participants would be identified. The Researcher stated they have a single cancer centre in the region that all patients with lung cancer are referred to for chemotherapy. The Researcher stated if any patients were eligible they would have the study discussed with them at clinic.

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

1. The Committee queried an item on the PIS about receiving a lay summary ‘unless notified’ by a doctor. The Researcher stated the intention was an option for a participant’s doctor to explain the results to them rather than an article. The Researcher stated this would be removed.
2. The Committee requested information explaining the questionnaires be added to the PIS as it does not currently include this under the “What do I do on my own?” section on page 5.
3. The Committee noted this was a very involved study and recommended including a flow diagram on the PIS to illustrate what is different to standard care and what changes participants will have by being part of the trial. The Committee stated it could be a simple demonstration of screening to induction to maintenance splitting off into different branches.
4. The Committee requested the statement on page 4 of the PIS that HIV and hepatitis MAY be reported be changed to MUST be reported as these are notifiable diseases.
5. The Committee advised that there was no consent on the consent form for samples to be sent overseas. The Committee requested a point adding this be included.
6. The Committee queried a statement on page 11 of the PIS discussing tumour tissue samples sent overseas and noted another reference in the application about blood going overseas. The Committee requested clarification as to what would be sent overseas. The Researcher stated they believe any blood and urine samples would be tested at the local laboratory and would revise the paragraph for clarity.
7. The Committee requested the Researcher ensure that it is clear in the PIS that participants have the right to request and correct information held about them in the study.

Decision

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

* Please amend the Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee. (*Ethical Guidelines for Intervention Studies* paragraph *6.22*).

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

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| **12** | **Ethics ref:** | **19/CEN/113** |
|  | Title: | Maxigesic IV Exposure Study |
|  | Principal Investigator: | Dr Simon Carson |
|  | Sponsor: | AFT Pharmaceuticals Ltd |
|  | Clock Start Date: | 11 July 2019 |

Dr Simon Carson 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 need addressing by the Researcher were as follows.

1. The Committee noted a reference to an American name for paracetamol on page 6 of the PIS. The Committee requested this be amended to paracetamol for consistency and local context.
2. The Committee noted a reference to the Southern HDEC on page 2 of the PIS. The Committee requested this be amended to state the Central HDEC.
3. The Committee noted the supplied insurance certificate expires on 31/0719. The Committee requested the Researcher ensure this is kept up to date.
4. The Committee requested the inclusion of contact information for the Health and Disability Commission and HDEC.
5. The Committee requested the addition of information advising participants of their right to access and correct the study’s information on them.
6. The Committee noted a statement regarding following a participant’s pregnant partner with no accompanying pregnant partner PIS. The Committee requested either a PIS for a participant’s pregnant partner or to remove the statement. The Researcher agreed to remove the statement.

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee.

## General business

1. The Committee noted the content of the “noting section” of the agenda.
2. The Chair reminded the Committee of the date and time of its next scheduled meeting, namely:

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| --- | --- |
| **Meeting date:** | 27 August 2019, 12:00 PM |
| **Meeting venue:** | Room GC.3, Ground Floor, Ministry of Health, 133 Molesworth Street, Wellington, 6011 |

No members tendered apologies for this meeting.

The meeting closed at 5:45pm