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| **Committee:** | Central Health and Disability Ethics Committee |
| **Meeting date:** | 22 October 2019 |
| **Meeting venue:** | Molesworth Conference Room, The Thorndon Hotel, 24 Hawkestone Street, Wellington |

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| **Time** | **Item of business** |
| 12:00pm | Welcome |
| 12:15pm | Confirmation of minutes of meeting of 24 September 2019 |
| 12:30pm | New applications (see over for details) |
| 12:30 – 12:55pm  12:55 – 1:20pm  1:20 – 1:45pm  1:45 – 2:10pm  2:10 – 2:35pm  2:35 – 3:00pm  3:00 – 3:25pm  3:25 – 3:50pm  3:50 – 4:15pm | i 19/CEN/171 (Helen W / Patries  ii 19/CEN/177 (Sandy / Peter)  iii 19/CEN/169 (Cordelia / Patries  iv 19/CEN/170 (Helen D / Peter)  v 19/CEN/172 (Sandy / Patries)  vi 19/CEN/173 (Helen W / Peter)  vii 19/CEN/174 (Cordelia / Peter)  viii 19/CEN/175 (Helen D / Patries)  ix 19/CEN/176 (Helen W / Patries) |
| 4:15pm | Substantial amendments (see over for details) |
| 4:15-4:25pm | i 16/CEN/136/AM04 |
| 4:25pm | General business:  Noting section |
| 4:30pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Mrs Helen Walker | Lay (consumer/community perspectives) | 01/07/2015 | 01/07/2018 | Present |
| 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 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 12:00pm 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 24 September 2019 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **19/CEN/171** |  |
|  | Title: | Testing Strategies to Minimise Stress Testing in Patients with Acute Chest Pain and Negative Cardiac Blood Tests in New Zealand (TACTICS-NZ) |  |
|  | Principal Investigator: | Dr MARTIN THAN |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 18 September 2019 |  |

Dr Martin Than and Dr Joanna Young 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. The study seeks to determine an optimal approach to select those patients who do and those who do not require an exercise tolerance “treadmill” test, when they present to the Emergency Department with chest pain or related symptoms but are deemed unlikely to be having a heart attack or related heart problems.
2. Current guidelines in New Zealand recommend performing exercise tolerance tests in patients to check for underlying coronary artery disease “narrowing the blood vessels supplying the heart”, unless patients are clearly very low risk. This is because a very small percentage of patients may have underlying coronary artery disease that may be able to be treated with stents or coronary artery bypass grafting. However, there is no universal consensus for the guidelines because there is weak evidence for benefit of testing and there can be false positive results, where patients may be exposed to unnecessary invasive testing.

1. Consequently, there are vast regional differences throughout New Zealand, with some hospitals performing exercise tolerance tests on all patients and some hospitals performing tests on very few patients. The researchers have developed a clinical decision rule that has been shown to safely identify up to 30% of patients who do not require an exercise tolerance test.
2. The researchers want to test whether using clinician judgement or the clinical decision rule compared to usual testing, can improve the identification of patients who require a treadmill test, in a Christchurch hospital-based study of approximately 1000 patients. Patients discharged from the Emergency Department and deemed lower-risk for a heart attack will be recruited. Those who decide to take part in the study will be randomly assigned to one of three approaches for deciding whether an exercise tolerance test is required. Patients can answer an optional 30-day satisfaction with care questionnaire. The researchers will follow-up patients’ health records to determine which approach for exercise tolerance testing works best.

Summary of resolved ethical issues

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

1. The Committee queried whether the precise (1017) number of participants was based on statistical powering. The Researcher confirmed it was.
2. The Committee advised that under New Zealand law verbal consent is inadequate and consent must be written. The Committee noted participants who perform the test would be able to sign but those who do not would not be able to give verbal consent over the phone. The Committee queried whether the study team could send consent forms to participants through the mail. The Researcher said the issue with mail was it was frequent for forms to be lost or never returned. The Committee stated that consent must be recorded in writing in order to comply with the law. The Researcher stated they are experiencing difficulties with the tension between an audit and research as they will be conducting an audit of CDHB’s practices but want to publish the findings and having to receive a written consent form from each participant in the mail would be a significant barrier.
3. The Committee queried why participants could not be consented while on the ward. The Researcher stated they could not ask routine clinical staff to neglect their duties in order to contribute to the research and go through the informed consent process with participants. The Committee suggested making the information sheet available to participants. The Researcher stated they would be happy to do this. The Committee suggested including a self-addressed and post-stamped envelope with the information sheet and then making a follow-up call to participants to remind them to post it. The Researcher stated this would invite the same problem as long-term follow-up and would likely have a very low response rate. The Researcher stated due to this the DHB has moved to a verbal model and follow-up is now generally performed over the phone.
4. The Committee stated that irrespective of the DHB policy the study must comply with the law and [Right 7(6) of the Code of Health and Disability Services Consumers' Rights](https://www.hdc.org.nz/your-rights/about-the-code/code-of-health-and-disability-services-consumers-rights/) states that informed consent to participate in any research must be in writing.
5. The Committee stated that although the code requires consent to be in writing it does not specify who has to write it. The Committee suggested that if the Researcher could obtain verbal consent over the phone and then keep a written record of the conversation including verifying the identity of the person spoken to then this could be a solution to allow verbal consent and be compliant with the code. The Researcher confirmed that a written record of the consent process would be kept in accordance with standard procedure.
6. The Committee suggested that after the phone call the study team send a transcript of the conversation obtaining verbal consent to the participant for their own records and to give them an opportunity to dispute what was said. The Researcher queried whether the study team would need to contact the participant again for this. The Committee stated they would not as the onus would be on the participant to get in contact if they had a problem with the transcript or no longer wanted to participate.
7. The Researcher raised the scenario of a participant losing the information sheet before the study team obtains the verbal consent. The Committee stated it was important to ensure that participants have all the necessary information in order to satisfy Right 7(6). The Researcher suggested the creation of an additional transcript to read over the phone to participants for the event that they have not read the PIS or lost their copy. The Researcher stated having a standardised template to go through would allow them to make everything absolutely clear in a lay manner. The Committee agreed this was a sensible approach and requested a copy of the transcript. The Committee stated this approach would also be advantageous to people who interact in an oral society with less of an emphasis on writing.
8. The Researcher queried whether they would require written consent for the two blood tests performed. The Committee advised that right 7(6) only requires written consent for research or an experimental procedure or when undergoing general anaesthetic. The Committee confirmed that the blood tests would not need a written consent, only participation in the research.

Decision

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

* Please supply a copy of the information sheet participants will take home.
* Please supply a copy of the simplified information sheet transcript a member of the study team will read over the phone in the event the participant has lost their information sheet.

After receipt of the information requested by the Committee, a final decision on the application will be made by Mrs Helen Walker and Dr Patries Herst.

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| **2** | **Ethics ref:** | **19/CEN/177** |  |
|  | Title: | Do latanoprost eye drops alter optic nerve stress signals in eyes with optic disc drusen? |  |
|  | Principal Investigator: | Mr Paul JY Kim |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 10 October 2019 |  |

Mr Paul JY Kim and Dr Jesse Gale 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. Optic disc drusen (ODD) are benign calcified deposits in the optic nerve that are generally inactive in adulthood but are thought to lead to gradual deterioration of peripheral vision. Some doctors treat ODD with glaucoma treatment to try to slow the rate of visual field loss, but there is no evidence to say it would be helpful or harmful.
2. This study aims to test whether glaucoma treatment increases or decreases stress signals in the optic nerve, in people with ODD.
3. The stress signals to be studied are electrophysiological signals called PERG and PhNR, which are recorded from the surface of the eye using a fine hair-thickness recording electrode, while the participant looks at checkerboard patterns or coloured flashes. The testing is all non-invasive, but the researchers will use anaesthetic drops and dilating drops in the testing.
4. The researchers plan to measure these signals from the optic nerve before and after a month of latanoprost eye drop treatment to lower the eye pressure.

Summary of resolved ethical issues

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

1. The Committee requested the Researcher give a brief overview of the study. The Researcher stated that drusen were relatively common in the population but there was no specific treatment. The Researcher explained they behave similar to glaucoma and it has been challenging to determine whether glaucoma treatment is beneficial for drusen as they change gradually over time and theoretically it could take 20 years to determine if the treatment is beneficial. The Researcher stated a new device has been developed that will potentially allow clinicians to measure a clinically relevant outcome and if glaucoma treatment is effective within a month. The Researcher stated if the early results of the trial were promising they could plan a more substantial trial or otherwise could present the data to show that glaucoma treatment is not effective for drusen.
2. The Committee noted the application stated that Māori would unlikely be in the research. The Committee queried the prevalence of drusen in Māori. The Researcher stated a population study of drusen in New Zealand has not been undertaken so the numbers are unknown. The Researcher stated data from overseas showed the condition was more common in those of European descent compared to those of Asian or African descent. The Researcher stated they have met most potential participants for the study and was not aware whether any were Māori but did not believe so. The Researcher stated the study has been submitted to the CCDHB’s Māori research advisory group and was awaiting a response and would incorporate any feedback.
3. The Committee noted the peer reviewer of the study was independent but had performed a very similar study previously. The Committee queried whether another reviewer would be worthwhile. The Researcher stated they could seek an ophthalmologist in Wellington or Auckland although they may not have the experience. The Committee stated it was preferable to get an expert that knows the equipment / technology than someone who does not and that the existing peer review would suffice.
4. The Committee queried whether the Researcher was planning to store the data on a central server or on a laptop hard drive. The Committee cautioned against the latter as if the laptop were stolen the Researcher would lose all the data. The Researcher agreed this was a valid concern and stated there would need to be a backup location. The Researcher stated the data would still be available on the recording instruments.
5. The Committee noted if identifiable data was still on the source instrument then it would not be accurate to say it is securely held on a laptop. The Researcher suggested they could use a study ID code instead of the patient identifiers on the instruments when collecting the images. The Committee agreed this was a sensible approach.
6. The Committee queried whether the potential participants would have sufficient vision to read the PIS. The Researcher stated that people with drusen have reasonable central vision in at least one eye and so they should be able to read it.
7. The Committee noted a treating clinician of the potential participants is on the research team and noted steps had been taken to avoid the suggestion of coercion, e.g. a third party to recruit participants. The Researcher stated they see patients in public and in private and have a list of those who have expressed interest in participating in research studies but confirmed another member of the study would consent the participants, so they do not feel like the study is part of their usual clinical care. The Committee accepted this.

Summary of outstanding ethical issues

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

1. The Committee noted the application stated data may be made available for future research. The Committee queried in what context the data would be made available. The Researcher explained they had in mind that they could provide anonymised data for people who want to scrutinise the study data and decide whether the electrophysiology signals had not been analysed properly. The Researcher stated that if they thought the results were encouraging, they may attempt a future study which could use this study’s data as a baseline. The Committee advised that this information was not in the participant information sheet or consent form and requested the Researcher amend these so participants consent to the use of their data in this way.
2. The Committee noted the answer in the application that cultural issues were not expected to arise. The Committee advised that the head is tapu and the research will need to accommodate cultural sensitivities. The Committee requested the Researcher be mindful of this in the future.
3. The Committee queried whether the Researcher had received feedback from the Save Sight Society. The Researcher stated this process was ongoing and they had not received it yet.
4. The Committee queried whether the Researcher was intending to use questionnaires. The Researcher stated they had been discussing the possibility and quality of life data may be useful as not many studies are done on drusen and none have evaluated drusen related quality of life. The Committee advised that if the Researcher was intending to use any questionnaires this would need to be explained in the PIS.
5. The Committee advised that if the Researcher intended to use the EQ-5D questionnaire they would need to have a safety plan in place for the event a participant indicated severe distress or suicidal ideation. The Committee stated a researcher cannot ask such questions to collect data and ignore the distress. The Researcher agreed this was important and stated they would first make a decision on whether to include the questionnaire or not and then make an amendment as appropriate.

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

1. The Committee queried a statement on page 4 of the PIS advising participants they can discuss with Dr Gale regarding continuing the eye drops. The Committee queried whether participants could receive the eye drops after the study’s conclusion if they required them. The Researcher confirmed participants could continue to have the eye drops prescribed if there was a clinical need.
2. The Committee requested the Researcher amend the phrase to specify participants can continue to receive the eye drops ‘if it is clinically appropriate’. The Researcher stated they had left it vague as they did not want to give the impression that the treatment should continue as it was not standard practice or to endorse a medicine that is not evidence based. The Committee stated it was not necessary to give the impression that everyone will receive them but to just add in a sentence reassuring participants that they can continue to receive access if it proves to be beneficial to them and they wish to continue using them.
3. The Committee noted the current ACC statement was out of date and requested the Researcher use the [latest statement available on page 3 of the HDEC template.](https://ethics.health.govt.nz/system/files/documents/pages/piscf-template-oct-2019-031019b.doc) The Researcher queried whether they would need to apply for ACC cover for the study. The Committee stated this would not be necessary and explained that as currently written it could be interpreted to mean that participants automatically get ACC coverage which is not the case. Participants need to understand that they are eligible *to apply* for ACC but their claim must be accepted by ACC and the Researchers cannot guarantee this.
4. The Committee requested the ‘yes / no’ boxes on the consent form be for items which are truly optional (i.e. the participant can answer NO and still participate in the study).
5. The Committee requested the inclusion of information explaining how long study data will be retained for and who will have access to it.
6. The Committee advised that participants have the right to withdraw at any time (and for any reason) and requested the PIS be amended to reflect this.
7. The Committee noted an option on the consent form for informing the participant’s GP. The Committee requested the addition of information explaining this in the PIS. Items should not appear in the consent form without accompanying information in the main information sheet.
8. The Committee noted the application mentioned there was a chance the signals may be worsened by treatment, but this was not stated in the PIS. The Committee requested the Researcher include this information so participants are aware of any and all risks.
9. The Committee requested the inclusion of detailed information on what participants can expect at study visits (e.g. reading charts, coloured lines, scans of the eye etc).
10. The Committee noted the application discussed primary and secondary objectives and suggested this would be useful information to include in the PIS.
11. The Committee queried the statement in the PIS that data will be stored on “one secure laptop” and noted that the Researcher should consider whether storing data on a single hard drive is appropriate.
12. The Committee requested the inclusion of information in the PIS about participants’ rights to not only access their data but also to seek correction of it under the Health Information Privacy Code 1994.

Decision

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

* Please update the Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee.
* Please supply a safety protocol for participants indicating distress if the questionnaires will be used.
* Please provide any feedback from the Save Sight Society and CCDHB Māori research group if available.
* Please update the data safety plan in the protocol.

After receipt of the information requested by the Committee, a final decision on the application will be made by Ms Sandy Gill and Dr Peter Gallagher.

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| **3** | **Ethics ref:** | **19/CEN/169** |  |
|  | Title: | Proof of Principle BCG Trial |  |
|  | Principal Investigator: | Professor Philip Hill |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 10 October 2019 |  |

Professor Philip Hill 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 is a proof of principle randomised trial of BCG versus placebo in medical and nursing students in one hospital in Bandung, Indonesia, to prevent conversion of an Interferon Gamma Release Assay (IGRA; reflecting new M. tuberculosis infection) over 12 months following the commencement of clinical training.
2. 150 students with IGRA and HIV negative results will be randomised to BCG vaccination/revaccination or placebo. They will be followed for 12 months with repeat IGRA test at 3, 6, 9, and 12 months. They will be given a logbook to record potential exposures to M. tuberculosis.
3. The study will inform the final design of a full-randomised trial powered to detect a difference in IGRA conversion between arms.
4. An interlocking immunological study will assess whether BCG vaccination/revaccination induces trained immunity in the students, with an extra sample taken at one month and three months post vaccination (n=100).

Summary of resolved ethical issues

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

1. The Committee noted the study was to take place entirely within Indonesia. The Committee queried why the Researcher had submitted the study for HDEC review as New Zealand law would not apply in Indonesia. The Researcher stated as the project was initiated in New Zealand the Indonesian authorities required New Zealand ethics to approve it before submission for ethical review in Indonesia.
2. The Committee expressed concern as part of its function was to assess relevant cultural issues to proposed research in New Zealand. The Committee stated it did not have expertise in potential cultural issues for Indonesian participants and this would limit its ability to review the study. The Researcher stated the Indonesian authorities would not need HDEC to review cultural factors as local review would cover this.
3. The Committee queried whether the Health Research Council was funding the study. The Researcher confirmed they partially were. The Committee noted reference to investigators from the Netherlands and queried the relationship. The Researcher explained there was an ongoing collaborative partnership with researchers in the Netherlands and Indonesia.
4. The Committee queried whether review was necessary from the Netherlands. The Researcher stated it would be regarded as being adequate for this study for the international review to be based in New Zealand. The Researcher stated he did not think the Dutch investigators would be seeking further ethical approval in the Netherlands.

Summary of outstanding ethical issues

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

1. The Committee explained that in New Zealand there are important Māori cultural considerations regarding blood to consider. The Committee advised the Researcher to consult with relevant Indonesian authorities to ensure any potential cultural issues with the proposed blood samples can be appropriately managed.
2. The Committee queried what insurance cover participants would be entitled to as ACC would not apply. The Researcher stated the Indonesian committee required that the study would cover any medical care for injury or accident occurring within the study. The Researcher stated Indonesia did not require a specific insurance policy. The committee expressed concern about this.
3. The Committee expressed concern about the proposed consent process. The Committee stated students may feel undue pressure to agree to participate as they may have a desire to be obliging or fear that refusal may affect their personal reputation, academic record or future employment. Additionally, if participants are excluded due to positive TB/HIV results this would be obvious to the rest of the student group. The Researcher stated students had actively approached the research group worried about TB exposure and the prospect of participation potentially mitigating the risk of TB is an attraction. The Researcher stated the research group are not generally involved in the direct training of students and if one or two are it would not be a problem to ensure the person engaging the students is not involved in their teaching and assessment.
4. The Committee noted the protocol referenced information on scheduled visits and reminders would be shared with the students’ coordinator. The Researcher stated the coordinator was not an investigator in the study. The Committee queried why the academic coordinator would receive private information on students. The Researcher explained this was necessary as the students would require formal permission (e.g. a letter) to be relieved from their regular duties in order to participate. The Committee requested an additional clause be added to the consent form for participants to agree to this.
5. The Committee queried the aggressive follow-up described on page 17 and the statement that contact attempts would be recorded in the participant’s file. The Committee queried whether this was their academic record, trial record or clinical record. The Researcher stated it would be the research study files only. The Committee requested this be clarified in the PIS.
6. The Committee queried the explanation of the electronic logbooks to record potential exposures to TB. The Committee noted a section about collecting info on direct contact with friends and family members with TB. The Committee advised that collecting information on people who are not participants makes them participants and they would need to consent to this. The Researcher stated they would not be collecting personal information on any of the friend / family members and it was more of a ‘yes / no’ question on exposure. The Committee requested this be made explicitly clear in the PIS.
7. The Committee expressed concern at the scenario of a participant learning they have a positive HIV result by opening an envelope without appropriate support. The Researcher stated there would be counselling available and the PIS was missing this statement. The Researcher agreed to amend the PIS. The Committee advised that it is critical to maintain confidentiality so no one else would learn a participant had a positive result and to provide appropriate support going forward. The Committee stated the PIS would need to explain all this so that participants understand the entire process in advance.
8. The Committee queried whether participants randomised to placebo would receive the vaccine at the end of the study. The Researcher stated this was not planned as the study was not powered to show evidence of protection. The Researcher stated if a future study proved this then it would be undertaken. The Committee queried whether or not that would affect participation rates. The Researcher stated they did not think it would.

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

1. The Committee requested the addition of information explaining where blood samples will be kept, for how long, what they may be tested for and how they will be discarded or destroyed.
2. The Committee requested the ‘yes / no’ boxes on the consent form be for items which are truly optional (i.e. the participant can answer NO and still participate in the study).
3. The Committee requested an additional section in the PIS to describe the genetic research and what tests would be involved (e.g. expression of certain genes in white blood cells) what the testing will and will not do (e.g. it will not sequence their whole genome and discover a genetic predisposition to certain diseases or any unexpected patrilineal revelations).

1. The Committee queried a statement on page 2 of the PIS. Under ‘what will my participation in the study involve?’ the third paragraph states if a participant’s test is positive no further examination is needed but then describes chest x-rays and sputum specimens. The Committee queried whether this meant participants who test positive are included or excluded from the study. The Researcher stated the further tests would not be part of the study but part of clinical care for a positive result because this would indicate the individual is at risk of TB disease. The Committee requested the Researcher clarify the section so participants understand what will happen if they test positive or not.
2. The Committee queried whether tuberculosis and HIV were notifiable diseases in Indonesia. The Researcher stated TB is but was uncertain whether HIV is officially notifiable. The Researcher explained if someone in Indonesia is thought to have TB they are referred to the national TB programme for a definitive diagnosis and treatment. The Committee stated this would need to be explicitly clear in the PIS and requested the Researcher add all the relevant information.
3. The Committee noted the application mentioned blood samples being sent to international laboratories. The Committee stated information regarding this including where they would be sent, how long they would be retained, what would happen to them thereafter would need to be in the PIS and participants would have to agree to their samples being sent overseas.
4. The Committee noted a discrepancy between the FUR PIS and consent form. The PIS states the samples may be used for future research on TB and the BCG vaccine whereas the consent form is agreeing for the sample to be stored and used for research of any type. The Committee stated these would need to be consistent. The Researcher stated they believed the intention related to future technology emerging. The Committee queried whether this was open consent to any FUR. The Researcher stated no it would be consistent with the research objectives of the study. The Committee requested the Researcher amend the consent sheet to align with the PIS and specify it as ‘optional future research’.

Decision

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

* Please update the Participant Information Sheet and Consent Form to allow participants to provide informed consent *(Ethical guidelines for intervention studies 6.13).*

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| **4** | **Ethics ref:** | **19/CEN/170** |  |
|  | Title: | COG AALL1731 |  |
|  | Principal Investigator: | Dr Lochie Teague |  |
|  | Sponsor: | Children's Oncology Group (COG) |  |
|  | Clock Start Date: | 11 October 2019 |  |

Dr Lochie Teague and Ms Sonia Alix were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. While outcomes in Standard Risk (SR) B-Lymphoblastic leukaemia (B-ALL) have improved significantly, this population still accounts for approximately half of the overall burden of relapse among children with ALL. Interventions that further reduce the number of SR ALL relapses will therefore significantly improve the long-term survival of the overall ALL population.
2. AALL1731 is a risk-stratified trial for children with newly diagnosed B-ALL and localised B-Lymphoblastic Lymphoma (B-LLy) that will test if the addition of blinatumomab to standard chemotherapy in patients with SR B-ALL at highest risk for relapse will improve disease-free survival (DFS).
3. Risk stratification will be determined by traditional prognostic factors (tumour genetics, extent of extramedullary involvement, early response to therapy as determined by flow cytometry) combined with the new DNA-based Minimal Residual Disease (MRD) detection technology of High Throughput Sequencing (HTS) of the immunoglobulin heavy chain (IgH).

Summary of resolved ethical issues

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

1. The Committee queried the duration of the trial and if the intention was to recruit 175 participants over 15 years. The Researcher stated the study had a long period of follow-up and clarified that the recruitment period is 5 years. The Researcher confirmed 175 participants was the recruitment goal, with 35 participants per year.
2. The Committee queried the proposed FUR as consent appeared to be sought in the main study consent form as well as an optional form. The Researcher stated it was repeated twice. The Committee stated this could potentially be confusing to participants. The Researcher stated they had created the separate form to satisfy HDEC’s preference, but COG also required it to be in the main PIS.

Summary of outstanding ethical issues

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

1. The Committee queried a statement on page 29 of the B-LLy PIS describing optional samples for biobanking being labelled with the participant’s name, date of birth and COG identifier. The following sentence then states the samples will be kept under a code and not the participant’s name. The Committee requested clarification. The Researcher stated this was from the COG template and samples sometimes require identifiers. The Researcher stated it was a COG requirement in case the sample needed to be retrieved for clinical purposes. The Committee queried why a study ID would not be adequate for this purpose. The Committee requested the Researcher investigate whether identifiers were mandatory and if so please provide a justification from COG for not de-identifying the samples. The Committee stated its standard expectation is for samples to be labelled with the study ID code and year of birth only.
2. The Committee raised concern that the statement in the PIS “Samples from publicly funded studies are required to be shared as broadly as possible” is potentially coercive in respect to influencing participants to consent to optional biobanking.
3. The Committee queried whether any young participants with Down syndrome would be consenting for themselves upon turning 16. The Researcher stated they were unsure, and it would depend on their cognitive ability. The Researcher stated some may be able to whereas others may not. The Committee stated they would need to assess each participant on an individual level to ascertain Gillick competence and there is an international movement toward supported decision-making. The Committee suggested the Researcher devise a simplified PIS and verbally discuss with participants so they can form a view on whether they wish to participate. The Committee cautioned against the assumption that Down syndrome would preclude the capacity to consent.
4. The Committee queried whether any statistics on the prevalence in Māori were available. The Researcher stated data from the cancer registry demonstrated that outcomes between Māori and non-Māori were identical, unlike some other forms of cancer. The Committee stated this information would have been good to include in the application when answering question P.4.1. and requested the researchers bear this in mind for any future applications.
5. The Committee requested the removal of the statement on samples from publicly funded studies being available as this is not applicable in New Zealand. The Researcher stated they would remove the statement if allowed by COG.
6. The Committee requested the Researcher ensure that all information sheets contain a section on privacy rights that explains to participants the right to access and correct information held about them.
7. The Committee noted the cultural paragraph was in some information sheets but not all. The Committee requested the addition of cultural information to all participant information sheets.
8. The Committee requested an additional clause to consent to samples being sent overseas for all applicable consent forms.
9. The Committee requested the inclusion of the tables present in some information sheets to all of them.

Decision

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

* Please update the Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee.

After receipt of the information requested by the Committee, a final decision on the application will be made by Ms Helen Davidson and Dr Peter Gallagher.

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| **5** | **Ethics ref:** | **19/CEN/172** |  |
|  | Title: | ACNS1721: A Study of the Drug Veliparib with Radiation Therapy in Patients with Newly-Diagnosed High-Grade Glioma (COG) |  |
|  | Principal Investigator: | Dr Stephen Laughton |  |
|  | Sponsor: | Children's Oncology Group |  |
|  | Clock Start Date: | 10 October 2019 |  |

Dr Stephen Laughton and Mrs Leanie Fourie were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. Recent studies have shown that paediatric high-grade glioma (HGG) have established distinct biological subgroups with differences in clinical outcome. In the past, however, eligibility for Children’s Oncology Group (COG) HGG studies have been based purely on histological diagnosis, leading to considerable differences in study patients in regards to actual tumour biology. As a result, these study populations included very high-risk tumours with a dismal outcome as well as favourable risk tumours, making the study results difficult to interpret.
2. This phase 2 trial will test whether using veliparib with radiation therapy followed by veliparib with temozolomide during maintenance therapy will be better than treatment with other therapies that do not contain veliparib to improve event-free survival in patients with newly-diagnosed HGG that are wild-type for (i.e., do not have mutations in) H3 K27M, IDH, and BRAF. This study will also include patients with IDH mutant tumours on a separate study arm.
3. The outcome of these patients will be compared to historical cohorts with closely matching clinical molecular features.

Summary of resolved ethical issues

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

1. The Committee queried whether any participates who turn 16 would receive the adult PIS. The Researcher confirmed when participants reach 16 they will be reconsented on the full consent form so would receive the standard main PIS.
2. The Committee queried the proposed FUR as consent appeared to be sought in the main study consent form as well as an optional form. The Researcher stated it was repeated twice due to a COG requirement, but they make this clear to participants.
3. The Committee queried whether a high-grade glioma may cause some cognitive impairment. The Researcher stated they take the child’s cognitive ability into account when doing the assent and the form would only be provided to children the study team felt would be able to understand it. The Researcher stated if a potential participant is felt to be too impaired to properly comprehend the form the study would be explained by the consultant and nursing staff and they would not be asked to sign the form but would be informed on a level they could understand. The Committee accepted the Researchers explanation and stated it trusted Starship to make the appropriate judgement.

Summary of outstanding ethical issues

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

1. The Committee queried whether the 7-10 PIS could be enhanced with pictures to aid comprehension as the text could be challenging for a 7-year-old to understand. The Researcher stated they had previously received advice from HDEC to not use pictures. The Committee requested the Researcher supply evidence of this and maintained its position that the inclusion of illustrations in the assent form would benefit younger readers.
2. The Committee requested the inclusion of a cultural tissue statement in both the main PIS form as well as the PIS for 11-15-year olds.
3. The Committee requested the addition of information regarding sending samples overseas to the main PIS.
4. The Committee noted a parental signature box on the consent form for 16-year olds. The Committee queried whether this was necessary, as if a participant is Gillick competent they would not require parental consent, and if not, the parental consent would remain valid until they turned 18. The Researcher confirmed this was the case. The Committee requested the removal of the parental consent.

Decision

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

* Please amend the participant information sheets and consent forms, taking into account the suggestions made by the Committee.

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| **6** | **Ethics ref:** | **19/CEN/173** |  |
|  | Title: | Cabozantinib with Nivolumab and Ipilimumab in Untreated Metastatic RCC |  |
|  | Principal Investigator: | Mrs Wendy Thomas |  |
|  | Sponsor: | Clinical and Regulatory Services (CARSL) Consultin |  |
|  | Clock Start Date: | 10 October 2019 |  |

Dr Alvin Tan 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. Renal cell carcinoma (RCC) is a type of kidney cancer. A study has shown that one-third of patients with previously untreated advanced or metastatic RCC of intermediate- or poor-risk benefitted from treatment with anti-cancer drugs called nivolumab (nivo) and ipilimumab (ipi). However, two-thirds of patients in that study showed little improvement. Those patients may benefit from taking nivo and ipi in combination with another anti-cancer drug called Cabozantinib, which affects a different part of the cancer than nivo or ipi.
2. In this study, 676 participants with "locally advanced or metastatic RCC of intermediate or poor risk" with clear cell classification will be recruited globally. They will be split evenly into two groups, which will be treated with either (1) nivo+ipi+cabozantinib, or (2) nivo+ipi+an inactive placebo.
3. The safety and effectiveness of these combination treatments will be assessed. Participants will be treated with ipi for 12 weeks, and with nivo for 2 years, cabozantinib/placebo for up to 2 years or until they no longer appear to benefit.

Summary of resolved ethical issues

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

1. The Committee queried whether a peer review from the chairman of the Sponsor is appropriate for independent peer review. The Researcher stated though it was not truly ‘independent’ the evidence behind the science is strong. The Committee noted the application would also go to SCOTT so an additional peer review would not be necessary.

Summary of outstanding ethical issues

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

1. The Committee advised that for future applications when answering question P.4.1. it would be helpful to include statistics of the prevalence of the disease in Māori and the potential implications of the research on Māori. The Committee requested the Researcher bear this in mind for any future applications.
2. The Committee queried whether the study intended to collect information on a baby after their birth. The Researcher stated they were uncertain. The Committee noted the PIS included a statement about child health. The Committee advised the Researcher that in order to collect information on the child after their birth a parent/guardian would have to consent on behalf of the child once the child was born. The Committee suggested an additional consent box on the pregnant participant consent form for this purpose. The Researcher stated the average age of diagnosing renal cell carcinoma was 50 – 60 and they had not treated anyone of child bearing age but will check with the Sponsor to cover all potential scenarios.
3. The Committee noted the Sponsor’s liability insurance expires on 15/11/19. The Researcher agreed to follow this up.
4. The Committee advised that if the Researcher intended to use the EQ-5D questionnaire they would need to have a safety plan in place for the event a participant indicated severe distress or suicidal ideation. The Committee stated a researcher cannot ask such questions to collect data and ignore the distress. The Committee queried the plan for assessing the results of the EQ-5D questionnaires. The Researcher agreed that if they would be collecting that information, they would need to action any concerning results. The Researcher stated the data would be manually put in the clinical record and the study coordinator would be responsible for this. The Researcher agreed to revise the protocol to clarify the response to concerning results.

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

1. The Committee requested clarification on where the tumour samples would come from and what would happen to them in the study. The Researcher stated most participants would have had a nephrectomy or renal core biopsy which are sent overseas for electron microscopy testing. The Researcher stated eventually genetic testing for subtyping may be done. The Researcher stated they were uncertain what would happen to the tissue afterward and would seek clarification. The Committee requested this information be added to the PIS.
2. The Committee noted the consent form included a clause consenting to standard tissue disposal and another statement on consenting to storage and use. The Committee requested this be amended.
3. The Committee requested the inclusion of a cultural tissue statement in the FUR PIS. [An example can be found on the HDEC website.](https://ethics.health.govt.nz/guides-templates-forms-0/human-tissue-use-%E2%80%93-guidance) The Researcher stated this was omitted due to the study being an international collaborative trial and agreed to produce a localised version containing the relevant cultural information.
4. The Committee requested the ‘yes / no’ boxes on the consent form be for items which are truly optional (i.e. the participant can answer NO and still participate in the study).
5. The Committee noted an error in the PIS with the same table repeating on pages 5 and 9.
6. The Committee noted the statement on page 12 informing participants that other cancer treatments are prohibited while on the study. The Committee requested an additional statement informing participants that pain relief will still be available to them as this may be of prime concern.
7. The Committee noted the genetic research section did not contain information on any potential risks. The Researcher stated there was no genetic testing planned and only the original histology would be reviewed. The Committee stated page 13 of the PIS discusses genetic testing and de-linking. The Researcher stated they believed this referred to biomarkers and not a genetic panel. The Researcher agreed to seek clarification and amend the sheet.
8. The Committee noted the reproductive risks in the PIS only recommended condoms for male participants. The Researcher stated men must use condoms and women must use a dual process e.g. oral contraceptive plus barrier method. The Committee recommended the Researcher [adapt the HDEC reproductive risks template](https://ethics.health.govt.nz/system/files/documents/pages/template-for-reproductive-risks-in-participant-information-sheets-sep17.docx) to ensure participants understand the requirements.
9. The Committee noted an option on the consent form for informing the participant’s GP. The Committee requested the addition of information explaining this in the PIS. Items should not appear in the consent form without accompanying information in the main information sheet.
10. The Committee requested the addition of an optional Future Unspecified Research participant information sheet and consent form for participants to opt-in to and recommended the Researcher consult the [HDEC FUR template](https://ethics.health.govt.nz/system/files/documents/pages/fur_piscf_template.doc).
11. The Committee requested the researcher add ‘Lead Maternity Carer’ to the options for discussion on the pregnant partner PIS.
12. The Committee requested the inclusion of the [ACC statement available on page 3 of the HDEC template](https://ethics.health.govt.nz/system/files/documents/pages/piscf-template-oct-2019-031019b.doc) to the pregnant partner PIS.
13. The Committee advised that the option for a legally authorised representative for the pregnancy follow-up program is inconsistent with New Zealand law. The Researcher agreed to remove it.
14. The Committee noted a statement on page 3 of the PIS advising that if a participant has to discontinue, they could not know which drug they were receiving. The Researcher stated they would unblind a participant for safety reasons and in an emergency the study doctor would know which drug the participant received. The Researcher speculated the sentence was intended to mean that a participant could not find out by themselves and only through the emergency safety protocol. The Committee requested this section be clarified as a layperson could interpret it to mean the study doctor will find out and then withhold this information from them.
15. The Committee noted the privacy statement on page 25 of the PIS could be potentially confusing and requested it be clarified so participants can easily understand. The Committee recommended the Researcher consult the HDEC template.
16. The Committee requested an additional statement in the consent form advising participants of their right to access and correct information held about them.
17. The Committee requested an update to the PIS to inform participants that they will be asked to complete quality of life questionnaires and if anything arises where they may need extra support the study team will contact their GP.

Decision

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

* Please update the Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee.
* Please update the protocol to include a safety plan for the event of a participant indicating severe distress.
* Please include a separate PIS for Future Unspecified Research.

After receipt of the information requested by the Committee, a final decision on the application will be made by Mrs Helen Walker and Dr Peter Gallagher.

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| **7** | **Ethics ref:** | **19/CEN/174** |  |
|  | Title: | A study to evaluate the safety and tolerability of seladelpar in subjects with primary biliary cholangitis |  |
|  | Principal Investigator: | Dr. Jing Hieng (Jeffrey) Ngu |  |
|  | Sponsor: | CymaBay Therapeutics, Inc. |  |
|  | Clock Start Date: | 10 October 2019 |  |

Dr Jing Hieng Ngu was not present for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The study will include participants who participated in the previous PBC studies with seladelpar (CB8025-21629, CB8025-31735 (ENHANCE), or CB8025-21838) allowing their treatment to continue. Qualified participants who participated in CB8025-31735 (ENHANCE) and were receiving placebo, will be randomized 1:1 to seladelpar 5mg or 10 mg. Other subjects will not be randomized and continue their seladelpar treatment dose.
2. Potential adjustment of dose from 5 to 10 mg to improve biochemical response will be considered and potential adjustment of doses for safety or tolerability will be managed.

Summary of outstanding ethical issues

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

1. The Committee requested an explanation of what “prohibited medications” are on page 4 of the main PIS so participants understand what they can and cannot take.
2. The Committee advised that opt-out consent for Future Unspecified Research is not appropriate for research in New Zealand. The Committee requested the addition of an optional Future Unspecified Research participant information sheet and consent form for participants to opt-in to and recommended the Researcher consult the [HDEC FUR template](https://ethics.health.govt.nz/system/files/documents/pages/fur_piscf_template.doc).
3. The Committee noted a clause in the consent form to inform the participant’s GP but this was not discussed in the PIS. The Committee requested the addition of information explaining this as matters should not appear in the consent form.
4. The Committee noted a clause in the consent form agreeing to the use of data for study and scientific purposes including future use – The needs to be explained in the information sheet- preferably a separate FUR PIS.
5. The Committee recommended a proof-read to check font and formatting consistency.
6. The Committee requested the addition of information explaining compensation provisions in the PIS. An example can be found in the [HDEC PIS template.](https://ethics.health.govt.nz/system/files/documents/pages/piscf-template-oct-2019-031019b.doc)
7. The Committee noted page 2 of the pregnant partner form referencing ‘your country’. The Committee requested this be changed to state New Zealand.
8. The Committee advised that under New Zealand law a child has no legal status until birth and an additional consent from a parent/guardian will be required after the child is born to collect any health information on the child. The Committee suggested an additional consent box on the pregnant partner consent form to accommodate this.
9. The Committee requested the Researcher amend the pregnant partner PIS to also cover the scenario of a pregnant participant.
10. The Committee requested clarification of the clause consenting to “data obtained in this programme including newborn child’s coded medical information be retained and used for future research in study subjects…”. The Committee advised that any proposed opt-out future research in the pregnant partner PIS would need to be presented as an optional FUR PIS. Additionally the child must reconsent upon reaching the age of 16.
11. The Committee requested the PIS be localised for a New Zealand context (e.g. change ‘subject’ to ‘participant’, ‘FDA’ to ‘Medsafe’ etc).
12. The Committee advised that the option for a legally authorised representative on the pregnant partner form is inconsistent with New Zealand law. The Researcher agreed to remove it.
13. The Committee commended the Researcher for including relevant Māori statistics in the application when answering question P.4.1. The Committee advised that Māori perspectives on blood and tissue are relevant issues that should have been included in P.4.2. The Committee requested the Researcher bear this in mind for any future applications.
14. The Committee requested that if a pregnant partner’s blood is to be sent overseas there is an additional clause in the pregnant partner form consenting to this.
15. The Committee requested the reference to the STH HDEC on page 14 of the main PIS be amended to state the Central HDEC.
16. The Committee requested the inclusion of a cultural tissue statement in the pregnant partner PIS. [An example can be found on the HDEC website.](https://ethics.health.govt.nz/guides-templates-forms-0/human-tissue-use-%E2%80%93-guidance)
17. The Committee requested the addition of a common measure (i.e. ‘X tablespoons of blood’) when discussing the blood draw on page 7 of the PIS.

Decision

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

* Please update the participant information sheet and consent forms, taking into account the suggestions made by the Committee.

After receipt of the information requested by the Committee, a final decision on the application will be made by Dr Cordelia Thomas and Dr Peter Gallagher.

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| **8** | **Ethics ref:** | **19/CEN/175** |  |
|  | Title: | WO41554: Phase III in CDK4/6 inhibitor experienced PIK3CA mutant HR+/HER2- metastatic breast cancer |  |
|  | Principal Investigator: | Dr Sheridan Wilson |  |
|  | Sponsor: | Roche Products (New Zealand)Limited |  |
|  | Clock Start Date: | 10 October 2019 |  |

Dr Sheridan Wilson and Mrs Pallavi Wyawahare 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. The study is conducted to determine the safety and efficacy of GDC-0077 plus palbociclib and fulvestrant vs placebo plus palbociclib and fulvestrant in patients with PIK3CA-mutant hormone receptor positive, HER2 negative locally advanced or metastatic breast cancer.
2. Approximately 400 patients will be recruited worldwide. Patients will be screened for PIK3CA mutation through central testing to determine the eligibility. Once eligible, they will be randomised to receive GDC-0077 / placebo orally every day, palbociclib 21 days oral administration followed by 7 days off and fulverstrant on D1 and D15 of Cycle 1 and then Day 1 of each subsequent cycle.
3. Participants will continue to receive the drugs until they progress. Upon progression they will be followed for post treatment tumour assessment every 8 weeks for first 2 years and then every 12 weeks thereafter.
4. All patients who discontinue treatment permanently will if they consent be followed for safety for 30 days after final study treatment. Patients with hyperglycaemia will undergo additional safety follow-up assessments each month for up to 3 months.
5. Pre-treatment tumour tissue sample (fresh or archived) will be collected during screening visit along with blood collection for testing multiple biomarkers at respective visits per protocol.

Summary of resolved ethical issues

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

1. The Committee noted a discrepancy with the site planning to keep the study information for 15 years and the Sponsor planning to keep it for 25 years. The Researcher stated they were not sure of the reason and believed the site was following GCP guidelines. The Researcher suggested the site could keep the information for 25 years to be consistent.
2. The Committee noted a clause in the consent form consenting to photographs. The Committee queried whether participants would be identifiable from these photos. The Researcher confirmed they would not be.
3. The Committee noted the study intended to retrieve archival tissue samples from the DHB lab. The Committee queried whether they would only be accessing participants’ samples. The Researcher confirmed they would and confirmed they would not receive tissue from anyone that has not consented to be in the research.
4. The Committee queried whether the trial had protocol-specific insurance. The Researcher confirmed it did and the trial number was present on the certificate.

Summary of outstanding ethical issues

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

1. The Committee advised that if the Researcher intended to use the quality of life questionnaires they would need to have a safety plan in place for the event a participant indicated severe distress or suicidal ideation. The Committee stated a researcher cannot ask such questions to collect data and ignore the distress. The Committee requested the Researcher devise a safety plan for appropriate support and/or referral.

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

1. The Committee requested a more lay-friendly study title for the PIS.
2. The Committee noted the pre-screening PIS read as if it involved Future Unspecified Research on page 7. The Committee queried what samples were mandatory tests in the main study and which were optional. The Researcher stated these were part of the main study and there are separate consent forms for optional testing. The Researcher stated participants may consent to the optional samples being retained in storage for future research. The Committee requested an amendment to the PIS to make what is part of the main study and what is optional FUR explicitly clear to participants.
3. The Committee requested the consent form on page 11 be retitled to ‘Pre-Screen Consent Form’ as with multiple sheets it can get confusing. The Committee requested all the statements for the pre-screen visit correctly refer to it as a pre-screen and not the study itself. The Committee noted that all consent forms need headings so it is clear what they relate to.
4. The Committee requested the removal of information not relevant to the pre-screening period from the pre-screening PIS and consent e.g. pregnancy, informing the GP as these are not important until a participant is actually on the trial.
5. The Committee queried what health information the study would be seeking from the baby of a pregnant partner / participant. The Researcher stated the Sponsor agreed not to collect any information on the baby, only the pregnancy. The Researcher agreed to remove the collection of the baby’s health information from the PIS.
6. The Committee requested an additional section in the pregnant partner PIS discussing any potential risks, such as those risks set out in the main PIS.
7. The Committee requested the removal of the ‘on behalf of’ on the pregnant partner form as only the pregnant woman can authorise the disclosure of her health information.
8. The Committee advised that the option for a legally authorised representative on the pre-screen consent page is inconsistent with New Zealand law. The Researcher agreed to remove it.
9. The Committee requested the inclusion of a cultural statement in the pregnant partner information sheet. [An example can be found on the HDEC website.](https://ethics.health.govt.nz/guides-templates-forms-0/human-tissue-use-%E2%80%93-guidance)
10. The Committee requested a clause in the pregnant partner consent form agreeing to any samples/data being sent overseas along with accompanying information in the sheet.
11. The Committee requested an update to the PIS to inform participants that they will be asked to complete quality of life questionnaires and if anything arises where they may need extra support the study team will contact their GP.

Decision

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

* Please update the Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee.
* Please update the protocol to include a safety plan for the event of a participant indicating severe distress.

After receipt of the information requested by the Committee, a final decision on the application will be made by Mrs Helen Davidson and Dr Patries Herst.

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| **9** | **Ethics ref:** | **19/CEN/176** |  |
|  | Title: | Study of the Oral Factor D (FD) Inhibitor ACH-0145228 in PNH Patients as Monotherapy and with an Approved C5 Inhibitor as Background Therapy |  |
|  | Principal Investigator: | Dr Peter Browett |  |
|  | Sponsor: | CNS Ltd |  |
|  | Clock Start Date: | 10 October 2019 |  |

Dr Peter Browett and Margaret Joppa were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This study will allow for patients enrolled in the ACH471-103 protocol to switch to treatment with the 2nd generation molecule, ACH-0145228. ACH-0145228 is an orally-administered complement factor D(fD)inhibitor being developed for the treatment of complement-mediated diseases. This drug has improved bio-availability, and patients will be able to dose twice a day instead of three times daily, which is expected to dramatically improve their symptom breakthrough and convenience.
2. Participants will dose for 84 days. At the end of dosing, if they are experiencing a benefit from the study drug, they will be offered a long-term extension study (if supported by clinical and non-clinical data). Those who do withdraw or do not go onto the extension study will have tapered dosing over 6 days and a final visit 28 days after the last dose.
3. As the results from the development and reproductive toxicology study is still ongoing, the protocol excludes females of childbearing potential at this time. Three of the 4 PNH patients in the ACH471-103 study may be switched to this study, with the 4th (CBP female) will switch once the reproductive toxicology study is completed.
4. The study may also enroll PNH patients who have been newly diagnosed, as well as PNH patients who are currently on eculizumab (Medsafe approved but not funded by Pharmac) but having a sub-optimal response.
5. The primary objective is to evaluate the change in haemoglobin at 84 days of treatment, relative to baseline.
6. Participants will remain on the study drug as long as they are benefiting from the treatment. Efficacy, safety, and quality of life measures will be assessed throughout the study.

Summary of resolved ethical issues

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

1. The Committee queried the recruitment process and whether participants receiving the first-generation drug would switch over completely. The Researcher explained there is one patient on the first-generation inhibitor and several on an extension protocol who will be offered the opportunity to switch to the 2nd generation drug, which has the advantage of two doses per day instead of three and is more efficacious. The Researcher stated there is a second group of newly diagnosed patients in New Zealand and they would be offered the chance to participate.

Summary of outstanding ethical issues

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

1. The Committee queried the plan for participant reimbursement. The Committee noted participants would receive a payment of $100 per visit (before tax) and will additionally be reimbursed for reasonable travel up to $100. The Committee queried whether this was in addition to the main compensation. The Researcher confirmed it was and stated participants would receive $100 per visit with additional travel / visit reimbursement. The Committee requested this be clarified on the information sheet.
2. The Committee queried the plan for the extension period and whether participants can receive access to the drug as the section is ambiguously worded. The Researcher stated the protocol allowed the Sponsor to terminate the study for safety reasons. The Committee stated it could be interpreted as meaning when the study stops participants will not receive the drug. The Researcher stated they believed it referred to the initial study. The Researcher stated if participants are responding they have an obligation to continue therapy. The Committee requested this be clarified so it is explicitly clear, and participants understand the options available at the end of the study.
3. The Committee queried who the homecare representatives were. The Researcher stated it was a visiting homecare service providing home nursing as a private enterprise. The Researcher stated it’s an option for participants who live rurally or would have inconvenience coming into the study site. The Committee requested confirmation this service was available and requested information explaining it be added to the PIS. The Committee noted the ‘what will I have to do?’ section states participants are required to visit the study site so this would also need revising.
4. The Committee queried whether Paragon Global CRS operated in New Zealand. The Researcher stated they were uncertain. The Committee stated it was acceptable to use a company like this as long as the required information is available, so participants understand what is happening.
5. The Committee advised that if the Researcher intended to use the EQ-5D questionnaire they would need to have a safety plan in place for the event a participant indicated severe distress or suicidal ideation. The Committee stated a researcher cannot ask such questions to collect data and ignore the distress. The Committee queried the plan for assessing the results of the EQ-5D questionnaires. The Researcher stated it would be entered into the Sponsor’s electronic data capture. The Committee queried what action the site staff would take. The Researcher stated they relied on patient honesty to report distress. The Researcher stated the trial centre is staffed 24 hours a day and the Principal Investigator would make a clinical decision, or if they were unavailable the co-investigator on duty. The Committee requested a protocolised safety plan to ensure appropriate support and / or referral is available to participants who indicate severe distress.
6. The Committee queried whether the pregnancy form intended to collect the outcome of the pregnancy only (i.e. live birth) or health information on the baby. The Committee advised the Researcher that in order to collect information on the child after their birth consent from a parent/guardian would be needed after the child is born. The Committee suggested an additional consent box on the pregnant participant consent form for this purpose.

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

1. The Committee queried whether this was a first in human trial. The Researcher stated it was not and a healthy volunteer dose escalation study has been completed. The Committee suggested it would be useful to include this information in the PIS so participants know it has been safely tested before.
2. The Committee requested the inclusion of a table detailing the schedule of appointments.
3. The Committee noted a lot of information was applicable to the USA and not relevant to New Zealand. The Committee requested a revision of the sheet to localise it to a New Zealand context.
4. The Committee requested the sentence on page 3 of the PIS about signing the consent form be reworded to say participants will be asked to sign ‘*the* consent form’.
5. Committee requested the inclusion of a cultural tissue statement in the pregnant partner PIS. [An example can be found on the HDEC website.](https://ethics.health.govt.nz/guides-templates-forms-0/human-tissue-use-%E2%80%93-guidance)
6. The Committee advised that the option for a legally authorised representative on the pregnant partner form is inconsistent with New Zealand law. The Researcher agreed to remove it.

Decision

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

* Please update the Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee.
* Please update the protocol to include a safety plan for the event of a participant indicating severe distress.

After receipt of the information requested by the Committee, a final decision on the application will be made by Mrs Helen Walker and Dr Patries Herst.

## Substantial amendments

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| **1** | **Ethics ref:** | **16/CEN/136/AM04** |  |
|  | Title: | Game for Health Level 2 |  |
|  | Principal Investigator: | Dr Hiran Thabrew |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 01 October 2019 |  |

Dr Hiran Thabrew was not present 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 resolved ethical issues

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

1. The Committee was satisfied with the amendment and had no ethical concerns with it.
2. The Committee requested the Researchers ensure the assent document will accommodate abilities of children younger than originally planned.

Decision

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

* Please ensure the assent form is appropriate for the younger audience.

## 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:

|  |  |
| --- | --- |
| **Meeting date:** | 26 November 2019, 12:00 PM |
| **Meeting venue:** | Room ?, Ground Floor, Ministry of Health, 133 Molesworth Street, Wellington, 6011 |

1. **Problem with Last Minutes**

The minutes of the previous meeting were agreed and signed by the Chair and Co-ordinator as a true record.

1. **Matters Arising**
2. **Other business**
3. **Other business for information**
4. **Any other business**

The meeting closed at 4:30 pm.