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| **Committee:** | Southern Health and Disability Ethics Committee |
| **Meeting date:** | 08 October 2019 |
| **Meeting venue:** | Sudima Hotel, Christchurch Airport, 550 Memorial Drive, Christchurch |

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| **Time** | **Item of business** |
| 12:00pm | Welcome |
| 12:15pm | Confirmation of minutes of meeting of 10 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 | i 19/STH/181  ii 19/STH/178  iii 19/STH/179  iv 19/STH/174  v 19/STH/182 |
|  | Substantial amendments (see over for details) |
| 2:35 – 3:00pm | i 17/STH/101/AM03 |
| 3:00pm | General business:  Noting section of agenda |
| 3:15pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Sarah Gunningham | Lay (other) | 05/07/2019 | 05/07/2022 | Present |
| Dr Devonie Waaka | Non-lay (intervention studies) | 18/07/2016 | 18/07/2019 | Apologies |
| Assc Prof Mira Harrison-Woolrych | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | Present |
| Dr Paul Chin | Non-lay (intervention studies) | 27/10/2018 | 27/10/2021 | Present |
| Professor Jean Hay-Smith | Non-lay (health/disability service provision) | 31/10/2018 | 31/10/2021 | Present |
| Mr Dominic Fitchett | Lay (the law) | 05/07/2019 | 05/07/2022 | Present |
| Dr Pauline Boyles | Lay (consumer/community perspectives) | 05/07/2019 | 05/07/2022 | Present |

## Welcome

The Chair opened the meeting at 12:00pm and welcomed Committee members, noting that apologies had been received from Dr Devonie Waaka.

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 10 September 2019 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **19/STH/181** |  |
|  | Title: | AcrySof IQ Vivity Extended Vision IOL vs. TECNIS Symfony and AT LARA Extended Depth of Focus IOLs |  |
|  | Principal Investigator: | Dr Dean Corbett |  |
|  | Sponsor: | Alcon Laboratories (Australia) Pty Ltd |  |
|  | Clock Start Date: | 26 September 2019 |  |

Dr Dean Corbett & Ms Naoko Chapman were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This is a multicenter, prospective, randomized, bilateral lens implant study.
2. The study evaluates the user acceptability of the AcrySof IQ Vivity Extended Vision IOL vs. TECNIS Symfony and AT LARA Extended Depth of Focus IOLs in bilaterally implanted participants.
3. Clinical assessments, including patient report outcomes among participants in the test group will be compared to those among participants in the comparator groups.

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 this study would be open to private health consumers only. The Researcher stated that the study would be open to anyone who was interested, and that potential participants outside of the clinic would be informed by advertising (to be submitted to HDEC for review).
2. The Committee queried whether a participant being given a non-study lens would result in any cost to the participant. The Researcher confirmed that there would be no cost to the participants at any point in the study.

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 stated that health research cannot be stopped for commercial reasons in a New Zealand context.
2. The Committee stated that, to manage any undue influence on potential participants, a research assistant or research nurse (i.e., someone associated with the study who is not the Coordinating Investigator or Surgeon), is the first to approach potential participants for recruitment, and is the one who will obtain consent for the study (the Surgeon must still obtain individual consent for the surgery itself).
3. Please clarify whether study results can be suppressed by the sponsor, and whether the sponsor can withhold study data.
4. Please ensure that it is clear to the GP and study participants that for a given participant, there is an end date for the GP to inform the researchers about changes to the participant’s health.
5. Please clarify that participants be made aware that their GP will report on changes to the participant’s health following the operation(s), and how long for.

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

1. The Committee stated that a simplified study title should be used on all participant-facing documents.
2. The Committee stated that the section of the PIS that states that participants will not be able to drive following study visits, should be in bold.
3. The Committee stated that the risks section of the PIS should be amended to include frequencies of risks, where possible.
4. The Committee stated that the Consent Form should be amended, so that any non-New Zealand specific information (e.g., regarding Social Security Numbers and the FDA) are replaced with New Zealand equivalents, or removed where there is no New Zealand equivalent.
5. The Committee stated that Section Ten of the PIS on injury and compensation should be amended to contain text in line with the HDEC PIS Template for commercial studies (i.e., remove information on Civil Actions).
6. The Committee stated that a sentence should be added to the Consent Form, stating that participants understand the compensation arrangements for the study.
7. The Committee stated that page eight of the PIS must be realigned with the rest of the document, which states that both eyes must meet requirements for participation.
8. Please amend the PIS/CF so that differences between the three types of lenses are clear to participants, for example that Vivity is newer compared to the other two lenses.
9. Please realign the text in the PIS and Investigator’s Brochure on how many patients the study treatment has been used with in the past.
10. Please remove the replicated paragraph in page ten of the PIS: “You do not have to participate in this study to receive treatment or your conditions. Alternative therapies for the treatment of your cataracts are available. This includes other approved IOLs which provide functional vision at the far distance only (monofocal IOL) or at multiple targeted distances (bifocal/trifocal IOLs) Rather that participate in this study, you may choose to be treated with alternative treatments. Please talk to your doctor about these and other options”.
11. The Committee stated that the PIS should clarify whether participants will receive the same or different types of lenses in each eye.
12. The Committee stated that the PIS and CF should be formatted and/or presented in a way that visually impaired participants are able to read and understand the entire document.

Decision

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

* Please provide advertising materials to HDEC for review
* Please confirm whether the study will be stopped for commercial reasons
* Please amend the study Protocol to ensure that no undue influence is placed upon potential participants during the recruiting and consent process
* Please clarify whether study results can be suppressed by the sponsor, and whether the sponsor can withhold study data.
* Please ensure that there is an end date for GP informing on changes to the participant’s health.
* Please clarify that participants be made aware that their GP will report on changes to the participant’s health following the operation(s), and how long for.
* Please make changes to the Participant Information Sheets and Consent Forms, taking into account the feedback provided by the Committee (above)

After receipt of the information requested by the Committee, a final decision on the application will be made by Dr Sarah Gunningham and Dr Paul Chin.

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| **2** | **Ethics ref:** | **19/STH/178** |  |
|  | Title: | Fusionless Scoliosis Correction Device in Children |  |
|  | Principal Investigator: | Mr Bruce Hodgson |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 26 September 2019 |  |

Mr Bruce Hodgson 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 protocol is to provide an outline for the introduction of a fusionless scoliosis correction device in the treatment of Adolescent Idiopathic Scoliosis (AIS), a spinal deformity that occurs predominantly in growing teenage girls.
2. The surgical implant device has been developed, modified and perfected in animal studies (sheep) over the last six years.
3. The device has already been implanted in 2 children with early onset scoliosis.
4. The reason for the development and introduction of this nonfusion device is to allow guided correction of the deformed spine in the adolescent idiopathic scoliosis group while preserving mobility and allowing natural growth of the spinal vertebra to occur in a controlled manner.

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 age range of the participants. The Researcher stated that participants will be between nine and sixteen years old, as they still have growth remaining.
2. The Committee queried the Researchers’ intention to share data in an identifiable form. The Researcher responded that sharing in this form will only occur within members of the study team.
3. The Committee queried how any potential conflicts of interest during study recruitment would be managed by the Researcher. The Researcher stated that, while they will be recruiting from their own patients, the Researcher will ensure that potential participants will be fully informed about the device and its stage of development. The Researcher stated that potential participants will be given enough time to go away and decide on their own if they want to participate, and no coercion will take place.
4. The Committee queried whether the questionnaire described in the protocol is standard in these instances. The Researcher responded that it is.

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 stated that researchers must receive assent from the child, in addition to consent from their parent/guardian, for them to participate in the study.
2. The Committee stated that participants will need to reconsent to their participation when they turn sixteen.
3. The Committee stated that there should be minimal difficulty for participants in seeking compensation or support if an adverse event takes place. Given the probability of future commercialisation of the trial device, ACC may not cover injuries or support for adverse events; in this instance, private, trial-specific insurance must be obtained by the Researcher. In the meantime, the Researcher should seek advice from their locality on the insurance status of the trial. The Committee will seek parallel legal advice on this issue.
4. The Committee stated that independent scientific peer review must objectively review the scientific merits and validity of the study design, not just the trial device.

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

1. The Committee stated that the start of the PIS should be amended to more clearly state how many people the study device has previously been trialled with, and the experimental nature of the device.
2. The Committee stated that individual, age-specific information sheets and consent/assent forms should be created for the study. For example: nine-to-eleven-year-old assent form, eleven-to-fifteen-year-old assent form; parent/guardian consent form for these two age groups; sixteen-year-old consent form and a reconsent for all partiicpants once they reach sixteen years old. The Committee encourages the use of the HDEC template for guidance.
3. The Committee stated that the main PIS should contain a more balanced description of potential risks and potential benefits of the device.
4. The Committee stated that the level of detail on risks associated with the device should be reflected in the PIS, particularly the parent/guardian Consent Form.

Decision

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

* Please clarify age-specific assent/consent processes in the protocol
* Please provide a legal opinion from the study locality regarding the insurance requirements for this study. The Committee will seek parallel legal advice
* Please provide age-specific assent/consent forms as described above
* Please make the requested change to the Participant Information Sheets and Consent/Assent Forms described above
* Please provide independent peer review on the study design

After receipt of the information requested by the Committee, a final decision on the application will be made by Dr Sarah Gunningham and Dr Paul Chin.

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| **3** | **Ethics ref:** | **19/STH/179** |  |
|  | Title: | (duplicate) RSV MAT-004 - a research study to vaccinate pregnant women against RSV and assess the incidence of RSV associated events in the children born to these mothers |  |
|  | Principal Investigator: | Dr Thorsten Stanley |  |
|  | Sponsor: | GlaxoSmithKline |  |
|  | Clock Start Date: | 27 September 2019 |  |

Dr Thorsten Stanley & Ms Marina Dzhelali were present by teleconference for discussion of this application.

Potential conflicts of interest

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

Dr Sarah Gunningham declared a conflict, as she Chaired the previous review of this application when it was reviewed at another HDEC. Mr Dominic Fitchett was nominated as Acting Chair for the duration of this review. to ensure quorum was upheld.

Summary of Study

1. GlaxoSmithKline is testing a new vaccine for pregnant women to protect their babies against RSV. This is the first time that this vaccine will be given to pregnant women.
2. Two doses of the vaccine will be tested: 60µg and 120µg. These doses have been given safely to about 125 women who were not pregnant.
3. The study is being done to make sure the new vaccine is safe for pregnant women and their babies, find out how well the vaccine can boost antibodies in pregnant women, if these are transferred to the baby and if so, how long the antibodies stay in the babies’ blood.
4. It also aims to find out how often pregnant women visit a health care provider and how often their babies get sick, due to a cold-like illness.
5. About 150 healthy pregnant women and their babies will take part in the study around the world.

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 participant’s GP will always be informed about their participation in the study. The Researcher confirmed that they will.
2. The Committee queried whether testing for Hepatitis B and Hepatitis C was routine for pregnant women. The researcher confirmed that it is standard.

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 stated that, if a patient has chosen to withdraw from the study, the Researcher and Sponsor do not have the right to continue collecting data on them (as this would qualify as continued participation).

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

1. The Committee requested that the evidence of risks and adverse reactions, as written in the Investigator Brochure, is added to the PIS.
2. The Committee requested more information in the PIS about any potential risks to the participant’s baby.
3. The Committee stated that, if this is the first instance of the study drug being trialled in pregnant women, that this should be stated at the beginning of the PIS (in the style of a first-in-humans trial, i.e. in bold, in a box).
4. The Committee requested that the patient-facing study title is amended to use more lay-friendly language.
5. The Committee requested that the purpose of the study is amended to state that it is looking at immune response, rather than just to vaccinate babies against RSV.
6. The Committee suggested reviewing the symbols and graphics next to the “purpose of research” text, for how easily a lay-person might interpret them.
7. The Committee requested that participant-facing documents are formatted to ensure that there is a clear space in text between the main body of text and footers.
8. The Committee requested that page four of the PIS is amended to state that home visits are taking place so that participants do not have to come to the clinic.
9. The Committee requested that the statement at the top of page six, about the participant’s doctor signing for them and their baby at the first visit is amended to acknowledge that the baby in unborn at this stage:

* “The study doctor will:

Sign this consent from with you, for both you and your baby (at screening visit)”

1. Please remove the yes/no tick option for whether the participant’s GP is informed about their patient’s participation in the study, as this is not optional.
2. The Committee requested that the yes/no option for retention of data but destruction of samples upon study withdrawal is removed, as this will always be the case.
3. The Committee requested that page fifteen of the PIS is reviewed and amended to use more lay-language where possible.

Decision

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

* Please amend the PIS/CF and Protocol to reflect that doctors are not obliged to report on participants health status after the participant has withdrawn from the study, and that the Researcher and Sponsor do not reserve the right to request health information from a participant or their doctor after they have withdrawn from the study.
* Please update the Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee.

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| **4** | **Ethics ref:** | **19/STH/174** |  |
|  | Title: | KETAMINE AND SPIDER PHOBIA |  |
|  | Principal Investigator: | Prof Paul Glue |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 26 September 2019 |  |

Prof Paul 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.

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

Summary of Study

1. Specific phobia is a type of anxiety disorder that is often characterised by fear and avoidance of exposure to objects of situations such as spiders, dogs or heights. It has a 12-month prevalence of 7.3% in New Zealand. Most treatment for specific phobias tends to be psychological, using graded exposure therapy. This has little long-term evidence of effectiveness and relapse is common. No drugs are approved for treatment of specific phobia. Availability of an effective drug treatment could be useful for phobic patients unable to access or unable to tolerate psychological treatment approaches.
2. Ketamine was developed as a general anaesthetic and is currently used for sedation and analgesia. In recent years its effects in psychological disorders has been noted, particularly as a fast-acting treatment for refractory depression and anxiety. We have recently identified that ketamine has dose-related effects on anxiety ratings for a specific phobia (blood/needle phobia).
3. Clinically, ketamine could be used therapeutically to manage phobic situations that interfere with health or business activities (e.g. needles; phobic patients getting medical/dental procedures; flying; phobic patients needing to travel by air).
4. We intend to confirm our earlier findings administering oral ketamine to patients with a common phobia, (spider phobia), using presentation of spiders using a virtual reality headset.

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 status of a previous application by the same Researcher, regarding a trial of Ketamine. The Researcher stated that the application in question did not proceed as it was not approved by SCOTT.
2. The Committee queried who holds the patent that was declared in the present application. The Researcher stated that Douglas Pharmaceuticals hold the patent, which has since been published as a dose-ranging, open-label study of patients with anxiety and depression.
3. The Committee queried whether the present application was in support of the Douglas patent. The Researcher stated that it was not, as the patent in question is for ketamine in tablet form, whereas the ketamine is the present study will be in liquid form.
4. The Committee queried whether SCOTT were reviewing this study. The Researcher stated that they were not, due to a previous bioequivalence study using the Douglas tablets.
5. The Committee queried whether the results, if the study treatment was found to be successful, would it be transferrable to other specific phobias, where the study intervention is more likely to have clinical utility (as the ketamine for spider phobia per se appears to have limited clinical utility). The Researcher stated that it is likely to, as currently the same behavioural treatment (graded exposure therapy) is used for all types of specific phobia.
6. The Committee queried the use of a psychoactive control treatment, rather than a placebo. The Researcher stated that the use of placebo would unblind the study.

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 stated that scientific peer review should be independent, i.e. from a professional outside of the Researcher’s department, who can critically comment on the scientific validity of the study. For example, the dose-response curves (Fear Questionnaire bs ketamine concentration) appear to be almost flat, raising the question of whether the study intervention is scientifically justifiable.

The Committee requested the following changes to the Participant Information Sheet and Consent Form, and where relevant the Protocol:

1. The Committee stated that the use of spider phobia as a model for specific phobia, and that the study may not result in treatment for spider phobia, should be declared in the PIS.
2. The Committee stated that the “Purpose of Study” section of the PIS should be amended to explicitly state that this study is using spider phobia as a model to possibly treat other types of phobias in the future, and that this may not include spider phobia.
3. Please remove subsequent text from this section on mood disorders, as this is not relevant to the proposed study on individuals with specific phobia.
4. The Committee stated that the patent related to previous HDEC applications from the Researcher should be declared in the PIS, under the “Who pays for the study” section.
5. The Committee stated that a randomised dosage pattern should be disclosed in the PIS.
6. The Committee stated that, to err on the side of caution, the Researcher should disclose to participants in the PIS that there is no data on food-drug interactions, and therefore they should fast on the day of taking the study drug/control. Similarly, to account for the tmax of the study drug, participants should be held for at least two hours post administration.
7. The Committee stated that the title of the PIS should be simplified to the header, to be more lay-friendly.
8. Please remove reference to male and female volunteers in the PIS, as it implies healthy/non-clinical sample of participants.
9. Please include the screening process in the PIS and replace the term “actively suicidal” with a more lay-friendly term, such as “at risk”.
10. Please replace the term “skin conduction” with “sweat response” in participant-facing documents.
11. Please remove the statement from the bottom of page four of the PIS, which reads “we believe there will be an improvement”
12. Please review the visit times throughout the PIS to ensure consistency across documents.
13. Please include timings for the screening process in the PIS.
14. Please amend the PIS to include which drugs potential participants will be tested for: recreational or prescription, or both.
15. Please amend the PIS to include a declaration of any potential conflicts of interest with regards to past studies involving the Researcher and ketamine.
16. The Committee stated the PIS should include a statement on the possibility for drug interactions with the participant’s existing medications, and that the participant should discuss this with the Researchers.
17. Please amend the PIS to include a cultural statement on the tapu nature of the head, in relation to placing the VR headset on the head of participant.

Decision

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

* Please provide evidence of independent scientific peer review
* Please make changes to the Participant Information Sheets and Consent Forms, taking into account suggestions made by the Committee above

After receipt of the information requested by the Committee, a final decision on the application will be made by Assc Prof Mira Harrision-Woolrych and Mr Dominic Fitchett.

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| **5** | **Ethics ref:** | **19/STH/182** |  |
|  | Title: | Efficacy and safety of WVE-210201 in ambulatory boys with DMD |  |
|  | Principal Investigator: | Dr Gina O'Grady |  |
|  | Sponsor: | PPD |  |
|  | Clock Start Date: | 27 September 2019 |  |

Dr Gina O’Grady and Ms 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 is a Phase 2/3, multi-centre, randomised, double-blind, placebo-controlled study to evaluate the safety and efficacy of WVE-210201 (suvodirsen) in boys with Duchenne muscular dystrophy (DMD).
2. DMD is caused by mutations in the dystrophin-encoding DMD gene. The mutations are most commonly deletions which prevent the production of dystrophin. Dystrophin is part of a protein complex that provides structural stability to skeletal muscle and protects the muscle from injury during function.
3. "Exon skipping" technology targets the faulty area of the gene, resulting in the production of a shorter, but functional protein, despite the genetic mutation. Eteplirsen, produced by Sarepta Therapeutics, was the first "exon skipping" therapy to be granted accelerated approval by the FDA in 2016. Suvodirsen represents newer generation exon skipping technology, expected to result in improved dystrophin levels.
4. Patients will be randomized in a 1:1:2:2 ratio to placebo 3 mg/kg, placebo 4.5 mg/kg, WVE-210201 3 mg/kg, and WVE-210201 4.5 mg/kg. Screening will include a baseline muscle biopsy and must be completed in 6 weeks of signing the informed consent. Treatment consists of either study drug or placebo once weekly for 48 weeks.
5. Safety and efficacy assessments will be performed over the course of the study, with a second muscle biopsy at Week 12, 22, or 46. After 48 weeks on treatment, patients will be offered treatment in the open-label extension study. If they do not, a follow up visit will occur. If a patient stops treatment before Week 48, safety and efficacy assessments will be performed at the early termination visit.

Summary of resolved ethical issues

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

1. The Committee commended the Researchers on their responses to the Online Form questions about cultural competency.
2. The Committee queried whether participants, for the days when they are meant to wear the device, will wear it around the clock. The Researchers stated that the device can be taken off at night time, or when bathing.

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 stated that the request from the Sponsor for participants to not discuss the trial is unenforceable. This request should also be differentiated from participants posting study-related information online or discussing their participation in the trial with their GP, or other healthcare practitioners involved in their clinical care.

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

1. The Committee requested that all participant-facing documentation are reviewed by the Researcher to ensure that they are written in a consistent and unified style.
2. The Committee stated that the Consent Form should be amended to clarify that participants are consenting to the entire 96 weeks of the study (initial 48 weeks followed by open label extension study), rather than reconsenting after 48 weeks.
3. Please ensure PIS is formatted so that headings are on the same page as their associated bodies of text.
4. Please ensure that the PIS is formatted so that there is clear visual separation between paragraph text and footers.
5. Please amend footers to use more simplified lay-language where possible.
6. Please ensure that there is enough spacing between paragraphs in the PIS, to maximise readability.
7. Please amend the bottom paragraph on page two of the parent/guardian PIS, to be broken up into multiple sentences.
8. The Committee stated that the Children’s PIS for five-to-nine-year-olds should be simplified taking into account the reading ability of this age group.
9. The Committee stated the title of Children’s PIS for five-to-nine-year-olds should be simplified.
10. The Committee stated that the Children’s PIS for ten-to-twelve-year-olds should read like a more complex version of the younger child’s PIS, rather than a simplified version of the adult’s PIS.
11. The Committee suggested adding an image of the study device to the five-to-nine-year-old’s PIS.
12. The Committee stated that the PIS should be amended to include whether the study device is standard of care, and if not, it should be described in the PIS with a picture and information on when it can be worn and when it can be taken off (refer to point 7 above).
13. Please amend the sections of the parent/guardian PIS that discuss whether their child will be able to continue the study treatment, so that they do not contradict each other and reflect the availability of the study drug i.e. page fifteen: “After the screening, treatment period, and follow-up period are completed, the study doctor will decide what medical treatment your son should receive. He may be invited to continue receiving treatment with WVE-210201 if further extension of this study is given approval. If the is the case, we will inform you separately.” Versus page sixteen: “WVE-210201 is at an early stage of development. Therefore, after the research finishes, you son will not be able to continue to receive WVE-210201”.
14. Please replace the product names Tylenol and Advil for the names by which they are commonly known in New Zealand.
15. Please amend the section of the PIS that states that this treatment has only been studied in a small number of boys; please add how many people have used this treatment and move the statement to the start of the PIS.
16. Please amend the adverse reactions section of the PIS to include known frequencies.
17. Please amend page seven of the PIS regarding sample identification, as data and samples received by the Sponsor should be fully de-identified.
18. Please clarify in the PIS that the Sponsor will only receive samples identified by study number, as well as year of birth or a sham date of birth (not actual date of birth).
19. The Committee stated that the Parent/guardian PIS should clarify that positive testing for Hepatitis B and Hepatitis C qualify as exclusion criteria for the study, and that positive test results for these diseases are notifiable New Zealand to the Ministry of Health.

Decision

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

* Please provide clarification on the Sponsor’s request for participants to not talk about the trial, and amend documents accordingly
* Please make changes to the Participant Information Sheets and Consent Forms, taking into account the suggestions made by the Committee above

After receipt of the information requested by the Committee, a final decision on the application will be made by Prof Jean Hay-Smith and Mr Dominic Fitchett.

## Substantial amendments

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| **1** | **Ethics ref:** | **17/STH/101/AM03** |  |
|  | Title: | MRD-Seq in AML |  |
|  | Principal Investigator: | Professor Peter Browett |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 13 September 2019 |  |

Professor Peter Browett & Ms Jane Wiley 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. Acute Myeloid Leukaemia (AML) in adults has a dismal prognosis despite modern intensive chemotherapy. AML is caused by malignant cells with a combination of different genetic lesions and so almost every AML case has its own, unique combination of mutations. Estimating the number of cancer cells remaining (the minimal residual disease, MRD) in patients after treatment, and monitoring the cancer with high sensitivity is crucial to administer the right amount of highly toxic chemotherapy treatment. Currently, MRD cannot be measured for most AML patients due to the technology, time and cost involved.
2. The MRD-Seq project is a collaboration between LabPLUS at Auckland Hospital and the Leukaemia & Blood Cancer Research Unit (LBCRU) University of Auckland (UoA), to develop this important diagnostic test using advanced molecular technologies. The pre-clinical steps are now complete, and the next phase will involve the testing and monitoring of samples from patients with AML and benchmarking the novel MRD-Seq technology against an established MRD method.
3. Patients will be asked to consent to paired peripheral blood (PB) and bone marrow (BM) samples to be taken on 4-5 occasions at routine BM collects, and after remission to give PB samples at 3-monthly intervals for two years. Residual diagnostic material will be used when available, or if not, extra samples will be taken at the time of regular collects.
4. Once validated, MRD-Seq will be introduced as a routine test for AML patients throughout NZ. It will vastly improve prediction of disease course, monitoring and treatment decisions in this devastating disease. It is also translatable to other tumour types and non-invasive blood-based cancer monitoring.

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 testing on samples that had already been collected would qualify as Future Unspecified Use of tissue. The Researcher stated that it would not, as the test being performed was related to the original reason for which the tissue was collected.
2. The Committee queried whether bone marrow sampling for this study was additional to sampling that occurs as part of standard of care. The Researcher stated that no additional samples would be collected.
3. The Committee queried the frequency of bone marrow sampling, compared to adults. The Researcher stated that there would be no more samples taken than with an adult patient.
4. The Committee queried whether bone marrow sampling would cause any distress to patients, compared to adults. The Researcher stated that sampling is routinely done under general anaesthetic, as part of standard of care.
5. The Committee queried whether testing on samples is one-off, or ongoing, as testing after the participant turns sixteen will require them to reconsent. The Researcher stated that only the initial sample will be tested, for a predetermined period of three years.
6. The Committee stated that study data must be stored for ten years after the youngest participant has turned sixteen.

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 stated that, if non-AML patients are excluded from the study, mention of them should be removed from the Protocol (see page eighteen).

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

1. The Committee stated that the section of the PIS on risks with bone marrow sampling should include details as to what the specific risks, even if those risks are minimal.
2. The Committee requested a lay-language title for patient-facing documents.
3. The Committee stated that the seven-to-ten-year-old PIS should be simplified to account for the age of participants reading it. The Committee suggested testing the document with non-participants of the same age for readability.
4. The Committee requested that it is made clear in the PIS that, if the child does not assent to participation, they will not take part in the research (even if parent/guardian consent has been obtained).
5. The Committee suggested amending the section of the PIS regarding use of personal pronouns (definitions of “you” and “me”, etc.) so that it is simplified for the target age group.

Decision

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

* Please amend the study Protocol, taking into account the suggestions described above by the Committee
* Please amend the study Participant Information Sheet(s) and Consent Form(s), taking into account the suggestions described above by the Committee

## Review of approved studies

## 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:** | 12 November 2019 |
| **Meeting venue:** | TBD |

The following members tendered apologies for this meeting.

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.

The meeting closed at 3:15pm.