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| **Committee:** | Southern Health and Disability Ethics Committee |
| **Meeting date:** | 13 April 2021 |
| **Meeting venue:** | Via Zoom Meeting ID: 965 0758 9841 https://mohnz.zoom.us/j/96507589841 |

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| **Time** | **Item of business** |
| 10.00am | Welcome |
| 10.15am | Confirmation of minutes of meeting of 09 March 2021 |
| 10.30am | New applications (see over for details) |
| 10.30-10.55am  10.55-11.20am  11.20-11.45am  11.45-11.55am  11.55am-12.20pm  12.20-12.45pm  12.45-1.10pm  1.10-1.25pm  1.25-1.50pm  1.50-2.15pm  2.15-2.40pm | i 21/STH/69  ii 21/STH/80  iii 21/STH/78  *Break*  iv 21/STH/75  v 21/STH/76  vi 21/STH/77  *Break*  vii 21/STH/74  viii 21/STH/79  ix 21/STH/70 |
| 2.40pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Sarah Gunningham | Lay (other) | 05/07/2016 | 05/07/2019 | Present |
| Dr Devonie Waaka | Non-lay (intervention studies) | 18/07/2016 | 18/07/2019 | Present |
| Assc Prof Mira Harrison-Woolrych | Non-lay (intervention studies) | 28/06/2019 | 28/06/2020 | Present |
| Dr Cordelia Thomas | Lay (the law) |  |  | Present |
| Dr Paul Chin | Non-lay (intervention studies) | 27/10/2018 | 27/10/2021 | Apologies |
| Professor Jean Hay-Smith | Non-lay (health/disability service provision) | 31/10/2018 | 31/10/2021 | Apologies |
| Mrs Helen Walker | Lay (consumer/community perspectives) | 19/08/2020 | 19/08/2021 | Present |
| Mr Dominic Fitchett | Lay (the law) | 05/07/2019 | 05/07/2022 | Apologies |
| Dr Patries Herst | Non-lay (intervention studies) |  |  | Present |

## Welcome

The Chair opened the meeting at 10.00am and welcomed Committee members, noting that apologies had been received from Mr Dominic Fitchett, Professor Jean Hay-Smith and Dr Paul Chin.

The Chair noted that it would be necessary to co-opt members of other HDECs in accordance with the Standard Operating Procedures. Dr Cordelia Thomas and Dr Patries Herst confirmed their eligibility, and were co-opted by the Chair as members of the Committee for the duration of the meeting.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

## Confirmation of previous minutes

The minutes of the meeting of 09 March 2021 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **21/STH/69** |
|  | Title: | A feasibility study to investigate individualised exercise prescription for people with cancer |
|  | Principal Investigator: | Ms Jessica Allan |
|  | Sponsor: | University of Canterbury |
|  | Clock Start Date: | 12 March 2021 |

Jessica Allan, Margaret Currie and Nick Draper were present by videoconference for discussion of this application.

Potential conflicts of interest

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

Sarah Gunningham declared a potential conflict of interest and the Committee decided to excuse her from discussion.

Summary of Study

1. This research will be a longitudinal design to assess the feasibility of an exercise intervention for people with early stage breast and colon cancer from the point-of-diagnosis throughout treatment (n = 30 / annum). Feasibility will be evaluated by the rate of loss to follow up (LTF; completion of intervention assessments) and attendance (ratio of total attended to planned treatments).

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 there was a disconnect between this as a feasibility study and statements in the application form and protocol, as outcomes and data analysis is discussed with evaluation on improving cancer-related negative outcomes and disease progression. The Committee noted that if the aim is to see if an implementation of an exercise regime in New Zealand cancer patients is feasible, the aim should not be to strive for evaluating the efficacy of the program.
2. The Committee noted their concerns that participants may be misled from statements in the participant information sheet that this study could produce results that show that exercise impacts cancer treatment and outcomes, when it should only state the benefits of this current study, and not the potential aims of any future studies their participation would go on to inform.
3. The Committee queried what the recruitment process looks like for potential participants. The researcher responded that this will depend on collaborations with surgery and oncology departments. The potential participants will hear about the study from the clinicians, who will sign that the potential participant can be included. The Committee requested clear guidelines about how these clinicians will describe the study, to avoid any suggestion that this study is part of their treatment pathway. An updated detailed protocol to avoid any doubt that there could be inducement or misleading of participants is required.
4. The Committee further suggested the importance of someone in the study being able to assess study eligibility, as the submitted documents infer that clinicians external from the study currently are assessing eligibility prior to individuals giving informed consent to participate, with no formal eligibility assessment occurring from within the study team. Potential participants are currently stated in documentation to meet inclusion criteria as assessed by the clinicians. The Committee requested amendment to the study documentation to clarify this process. Please clearly outline that clinicians are only asking if the potential participants are interested in the study and handing over details to contact the researchers.
5. The Committee emphasised that the protocol needs to meet National Standards 9.7 & 9.8 and lacks enough detail, especially in regard to the above points.
6. The Committee requested a new peer review to be performed on the amended protocol, as the current provided peer review has been written based on the previously declined protocol.

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

1. Please remove from the first page “you’re invited to take part in a study on the effects of exercise on cancer treatment and outcomes”. The statement on page 2 that this a feasibility study needs to be the first statement on the first page.
2. The participant information sheet does not outline the time involvement overall for the study. Please include this.
3. Please include a statement that shuttles for transport are provided.
4. The Committee requested the inclusion of a more detailed cultural tissue statement to the PIS. The Committee recommended the following statement: *“You may hold beliefs about a sacred and shared value of all or any tissue samples removed. The cultural issues associated with sending your samples overseas and/or storing your tissue should be discussed with your family/ whānau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult before participating in research where this occurs. However, it is acknowledged that individuals have the right to choose.”*
5. Interchangeable references to ‘doctor’ and ‘GP’ need to be clarified as it is not clear whether ‘doctor’ is referring to the GP or a specialist clinician.
6. The Committee noted that template wording had not been fully adapted to the study, such as inferences to future research being kept in from the template. Please remove anything that is not included as part of the study.
7. Please remove references to outcomes or impact on cancer treatment and progression, as this study is only focusing on feasibility of regime implementation, not the effect of the regime.

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 feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
* Please supply an independent peer review for the current version of the study protocol. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.26).*
* Please update the study protocol, taking into account the feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7 & 9.8).*

After receipt of the information requested by the Committee, a final decision on the application will be made by full Committee (online).

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| **2** | **Ethics ref:** | **21/STH/80** |
|  | Title: | DF-006-1001: A Phase 1 study of DF-006-1001 in Healthy Volunteers and patients with Chronic Hepatitis B |
|  | Principal Investigator: | Prof Edward Gane |
|  | Sponsor: | IQVIA |
|  | Clock Start Date: | 01 April 2021 |

Edward Gane was present by videoconference 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. Drug Farm have developed DF-006 as a potential treatment for Chronic Hepatitis B (HBV). This is the first clinical study where DF-006 will be given to humans. The main goal is to determine whether DF-006 is safe and well tolerated when given at different doses. We will also measure the levels of the drug at different times. This study will be conducted in 3 parts.

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 that participant information sheets and advertisements for Part 3 are not assessed or approved as part of this application and must be submitted as an amendment when appropriate. The Committee further stated that the data and tissue management plan described an inclusion of Future Unspecified Research (FUR) for Part 3. The Committee requested the statement regarding an extra sample being taken in Part 3 for an unspecified use is removed from the data and tissue management plan. After discussion with the researcher, the Committee stated that the Part 3 amendment would require review via Full Committee. Please ensure a formal summary of changes for the protocol amendment and a Part 3 PISCF in tracked changes form from the Part 2 PISCF are provided to the Committee, along with this original HDEC application letter.

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 some documentation states samples are kept for 15 years post study, and other documentation indicates samples will be destroyed at the end of the study. The researcher responded that samples sent overseas are stored for up to 15 years. The committee requested justification from the sponsor for why they are retained for this period of time.
2. In the application form, r.3.1 describes biomarker assays planned for this study. The Committee requested clarification on the breadth of the exploratory assays and what they are targeting, particularly if anything genomic is explored.
3. The Committee queried the statement in the data and tissue management plan (Section 11.1, table) that discusses genetic material collected having significance to Māori participants). The researcher stated that there is no genomic consent form, therefore this must be a mistake. The Committee requested this is taken out if it is not appropriate.
4. The Committee highlighted a discrepancy between the Data and tissue management plan stating tissue upon withdrawal of the study will be kept, while the application form states it will be destroyed. Please confirm and correct this discrepancy.
5. The Committee noted that the insurance certificate does not cover all potential participants in Part 2 and does not cover optional cohorts or Part 3. Please confirm that if the optional cohorts are being added, the insurance is updated accordingly.
6. The Committee queried whether relevant cultural consultation has been undertaken as the application form states various cultural/ethnic populations as being targeted. The researcher seconded that none had been undertaken. The Committee requested the researcher looks into seeking consultation with stakeholders from targeted groups.
7. The Committee noted the application form indicates all participants will receive a summary of the study results, and that this should be the participants choice. Please amend the information sheet to reflect this.

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

SAD & MAD

1. Please look at restrictions around alcohol and other lifestyle factors, many of them seem to end immediately post-dose for cohort A.
2. References to AB-836 and Arbutus that are not related to this current study should be removed.
3. Mention that SARS-CoV-2 (COVID-19) is a notifiable disease on page 12.
4. Safety aspects and risks, for a First-In-Human study, are not well explained. Please expand on the key risks and make these clearer.
5. Please amend, using the HDEC template about contraceptive advice to ensure the examples are New Zealand specific (<https://ethics.health.govt.nz/guides-templates-forms-0/participant-information-sheet-templates>)
6. On page 3, remove the statement that all health research involving humans is reviewed by HDEC.
7. Please review for spelling and typos.
8. Explain 'placebo' in lay terms the first time it is used.
9. Explain 'washout' in lay terms
10. On page 6 and 7, please rewrite the section about conmeds in lay terms (' 5 half-lives, nephrotoxicity, hepatotoxicity, anticoagulant, licensed physician, 'apparent risk of drug-drug interaction')
11. Please provide the planned payment for back-up participants.
12. Delete duplicate paragraph regarding risks of sending data overseas from storage subheading.
13. In the consent form, please include consent clause regarding acknowledgement of reproductive risks.
14. The MAD objectives for Part 2 are listed as single-dose and food-effect, and number of nights in-house is incorrect. Please check and amend.

Decision

Parts 1 & 2 of this application were *provisionally approved* by consensus, subject to the following information being received:

* Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
* Please supply a data and tissue management plan to ensure the safety and integrity of participant data *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 14.17).*

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

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| **3** | **Ethics ref:** | **21/STH/78** |
|  | Title: | The Effect of Food on ZN-d5 in healthy female volunteers |
|  | Principal Investigator: | Dr Chris Wynne |
|  | Sponsor: | Novotech NZ Ltd |
|  | Clock Start Date: | 01 April 2021 |

Chris Wynne, Cory Sellwood, Alex Cole and Richard Robson were present by videoconference for discussion of this application.

Potential conflicts of interest

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

Devonie Waaka declared a conflict of interest. After discussion, the Chair was satisfied the member could remain for discussion.

Summary of Study

1. This study will compare levels of ZN-d5 (a BCL-2 inhibitor) in the blood over time in healthy female volunteers, when the study drug has been taken on an empty stomach and when it has been taken after a meal.

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 why this is being undertaken by women of reproductive age. The researcher clarified that there is potential for testicular toxicity from animal studies so males are not included. The Committee stated that embryo toxicity and changes to ovarian function were noted as a risk in the application form / associated documents. The researcher responded that there are no overt risks from 2 doses, but that the participants are not allowed to become pregnant due to the unknown risk. The Committee requested that the effects observed on fertility (with a return of function over time) in the animal trials is outlined clearly in the participant information sheet.
2. The Committee further noted their concern with the drug in the target population and requested justification from the Sponsor on targeting women of reproductive age instead of another such as post-menopausal women.
3. Please use the term 'women' rather than 'females' in the adverts for this study.
4. The Committee noted the sponsor appears to be have access to identified information for purposes broader than that acceptable to the Committee. Please clarify the specific study purposes for which the Sponsor would have access to identifiable information and amend documentation accordingly.
5. The Committee requested information on the payment amount participants will receive be included in the application form and PISCF.

The Committee requested the following changes to the Participant Information Sheet (PIS) and Consent Form (CF):

1. On page 4 and 5, please amend contraceptive statement to state explicitly to state that participants are to use a highly effective method and a barrier method together, as opposed to “two of the methods below”.
2. The collection of pregnancy and pregnancy outcome information must be contingent on the participant providing additional optional informed consent. Ensure the PIS/CF is updated to clearly state this.
3. Please include an additional statement that this is being tested in healthy women only.
4. Please use the term 'participants' rather than subjects throughout the PIS
5. The risks section (Page 10) is unclear regarding what is meant by "these changes were reversible over time". Please clarify.
6. The risk of skin photosensitivity is alluded to but not fully explained. Please amend.
7. Please amend the word “alarming” to “concerning” in the risk section.
8. Please ensure the summary table of assessments is amended in lay-language. Any medical terms or technical language required should be explained in lay language at the time of first use.
9. Under ‘what will my participation involve’, please mention upfront that participants will be asked to stay on site.
10. The use of the word “generally” when referring to data and sample labelling is vague. Please amend.

Future Unspecified Research (FUR)

1. Please clearly explain genomic research in lay terms.
2. Please state whether the research may involve analysis of a persons’ entire genetic code.
3. The statement about genetic counsellors etc is confusing and not appropriate for this PISCF.
4. Please justify the sharing of genetic FUR results with the study site. If this is done, then the Investigator must give participants the opportunity to receive the results of abnormal results of potential clinical significance (for example, CYP testing may be of importance to the participant in terms of other DDIs).
5. Please delete 'generally' from the statement that samples will be labelled with participant code only. This should always be the case.
6. A maximum retention time must be provided for samples. If this is 'indefinitely', then state this clearly.
7. Access to identifiable information for FUR must be much more restricted. Many of the bullet points are not valid reasons for access to identifiable data (bullet points 2 and 4 in particular).
8. On page 3, please remove 'generally' from the statement that 'any future results will only carry your participant code'.
9. On page 3, please add a specific risk statement regarding the risk of re-identification with genomic research (including the risks of DNA matches to blood relatives / DNA databanks etc).
10. In the consent form, please justify the requirement to access medical records for FUR.
11. The consent form also states codes may be stripped from tissue retained for FUR. This must be clearly stated in the information sheet first.

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 feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
* Please provide justification for the current study population, given the Committee’s concerns for the risks it imposes when other populations could be used *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 8.16 & 8.17).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Full Committee (online).

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| **4** | **Ethics ref:** | **21/STH/75** |
|  | Title: | A Study to Investigate the Clinical Effectiveness and Safety of ARO-APOC3 in Adults with Severe Hypertriglyceridemia |
|  | Principal Investigator: | Dr John Baker |
|  | Sponsor: | Arrowhead Pharmaceuticals, Inc |
|  | Clock Start Date: | 01 April 2021 |

No one was present by videoconference 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 double blind placebo controlled study aims to recruit 300 participants over approximately 80 sites globally aims to evaluate the safety and efficacy of ARO-APOC3 in adults with severe hypertriglyceridemia and to select a dosing regimen for later stage clinical studies in this patient population. Eligible participants will be randomly assigned 3:1 to receive a subcutaneous injection of either (10mg, 25mg and 50mg) of ARO-APOC3 or placebo.

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 that the insurance certificate is New Zealand-specific but covers 3 different protocols. Please provide an insurance certificate that is specific to this protocol.
2. It is stated that mandatory bone marrow samples will be collected during the study in the application form, but this is not mentioned elsewhere in the application. Please clarify this statement.
3. Section 7.5 of the Data and Tissue Management Plan states that tissue will be used for unspecified purposes that are not medical or scientific. It must be made clear that any use of tissue for purposes outside those required to complete protocol objectives is subject to optional consent by the participant. Please also clarify what type of unspecified research will not have a medical or scientific purpose.
4. The Committee raised the following concerns/issues with the application form responses:
   1. r.5.4.1 The doctor-patient relationship may result in patients feeling undue pressure to participate in research conducted by their clinician. Explain how this will be mitigated during the recruitment process.
   2. p.2.1 Please ensure the initial approach re participation in a clinical trial for patients comes from a member of the participant's clinical care team. If interest is expressed, the research team may then make contact to discuss further.
   3. r.1.6. outlines withdrawal of individual participants; for future applications please discuss reasons for terminating the study as a whole. It is noted that the protocol has not specific stopping rules for the study, only for individual participants.
   4. f.2.1. Eligibility criteria require contraception use and restrict sperm donation, however there are no restrictions on egg donation. Confirm there is no risk associated with egg donation post IP administration or consider restricting egg donation.
   5. r.2.5. The Committee requested confirmation of the minimum time different forms of data will be stored. The Committee requested confirmation that health information gathered during the study is kept for at least 10 years, as this was unclear in the documentation.
5. The Committee requested a safety plan in the protocol for staff visiting participants in their homes, that addresses safety and cultural issues.
6. The Committee asked for clarification if it is anticipated that 2 doses of the medication is therapeutic.
7. The Committee queried if patients should be remunerated for their time and inconvenience.

The Committee requested the following changes to the Participant Information Sheet (PIS) and Consent Forms (CF):

All

1. Please ensure the lay title is used as the main title for the information sheets.
2. Ensure that, should a participant withdraw from the main study, they are specifically asked whether they also wish to withdraw consent for the use of samples for optional future research.
3. Please review all PISCFs for typos, repetition and layout/formatting.

Main PIS/CF

1. Please make the following changes to the table on page 4:
   1. Review for lay terms (extremities, neurological status, respiratory system, antibodies, early termination);
   2. Provide NZ-specific advice regarding notifiable diseases or delete (discussed on page 11).
2. It is stated under the purpose of this study that this has already been tested previously in participants with hypertriglyceridemia in the second paragraph, then states further down that the side effects in people with elevated triglycerides is still being studied. Please reconcile these statements to avoid confusion.
3. Do not use phrase ‘dummy injection’ to describe a placebo.
4. On page 7, please limit discussion of optional research to the statement in bold. Delete additional reference in the table on p4-5, the remainder of the text on p7, the samples section on p9-10, blood draw section on p11, and MRI risks on p12.
5. On page 8, please ensure the GP is informed of / included in any instruction or discussion about discontinuing prescription medicines in order to participate in the trial.
6. The Committee noted that participants should not be left out of pocket for participating in research. The Committee queried the statement on page 9 that some side effects may require participants to pay for medication to treat.
7. On page 10, please explain what 'elevated liver enzymes' may mean in lay terms
8. The Committee noted that not all the methods of contraception listed are highly effective, such as condoms and some hormonal contraception methods. Please amend accordingly.
9. The Committee noted the HDEC approved compensation statement has been modified. Please remove the second paragraph from the compensation statement.
10. On page 11 under Hepatitis Testing, please amend “may inform” to “will inform” as this is a requirement, not an option.
11. The Committee noted that New Zealand does not consider ethnicity and geographic ancestry to be 'sensitive information'. Please amend and clarify what geographic ancestry is.
12. Collection of full date of birth and provision to the Sponsor as part of the de-identified data is not permissible. Age and year of birth only are permitted. Please amend.
13. Please state more clearly on page 17 who may have access to identifiable vs de-identified (coded) data.
14. In addition, the stated future uses of data ('relating to the study drugs') is very different to the scope stated in the Data and Tissue Management Plan. Ensure information is consistent.
15. Delete redundant information on page 18 regarding ownership of information (provided earlier in the PIS/CF)
16. Please include risks of sending data overseas; and risk of confidentiality / privacy breach.
17. In the consent form, please amend to state that only year of birth will be provided to the Sponsor
18. The Committee stated that the study may not be stopped for commercial interests and to make this clear on page 15.

MRI PIS/CF

1. Delete statement about costs from page 2 as it is stated in full on page 3.
2. Some statements on page 2 are yet to be completed or are highlighted in blue. Clarify what is intended for these sections.
3. Repeated statements on page 3 about voluntariness are redundant. Include once.
4. The Committee noted on page 3 that it is the Investigator's responsibility to contact the participant's GP or primary healthcare provider in the event of an incidental finding of potential clinical significance.
5. On page 4, please state clearly whether the imaging data may be used for future research not directly related to the current study.

Future Unspecified Research (FUR) PIS/CF

1. Please explain genes and genomic research in lay terms
2. Please state in lay terms whether genomic research may involve analysis of the participant’s entire genetic code (whole genome analysis)
3. Please clarify 'your personal information will not be attached to the sample'. The Committee queried if this is referring only to identifiable information or will no health information be linked to the sample.
4. Include the risks of privacy / confidentiality breach, particularly for genomic samples (see PG PIS/CF)
5. Include the risks of sending tissue overseas.
6. In the consent form, please include a clause stating that genomic research will be conducted.
7. Page 1 states that only a small number of participants from the main study and page 2 states all participants from the main study. Please correct as appropriate
8. Need to state the address to where samples are to be sent
9. Genetic research is an area of prime sensitivity for Māori because of the association with whakapapa. The Committee requested a cultural statement to acknowledge these concerns. The standard statement may be used and adapted: *“You may hold beliefs about a sacred and shared value of all or any tissue samples removed. The cultural issues associated with sending your samples overseas and/or storing your tissue should be discussed with your family/ whānau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult before participating in research where this occurs. However, it is acknowledged that individuals have the right to choose.”*

PG PIS/CF

1. The breadth of research for which participants are consenting is unclear. One statement reads “The study doctor seeks your permission to store your blood sample for future pharmacogenomic research relating to this study only. In the future, the sponsor, Arrowhead Pharmaceuticals, Inc., may use your blood sample to learn about many different diseases and conditions”. These are two very different things.
2. Please explain in lay terms whether the genomic research may include whole genome analysis (WGA). Provide more information about the genetic research to be undertaken.
3. The level of identification of samples is unclear in the document. Page 2 states that participants will not benefit from results because 'the link between you and your blood sample will be removed before your DNA is analysed'. Page 3 states that 'the sample will be identified by a code number to maintain your anonymity'. Please amend for consistency.
4. The statement 'neither your name no initials will be used on any forms or samples, therefore guaranteeing anonymity' is not appropriate. Please remove.
5. Include the risk of confidentiality / privacy breach - including risk of re-identification or DNA databank matching if WGA is planned (including risks to blood relatives).
6. Include risk of sending tissue overseas.
7. The statement regarding banking of health information is confusing. Please clarify if the 'personal health information' referred to is identifiable or de-identified data.
8. Please explain that genes are similar between family members
9. If the blood is being sent overseas, ethics approval will also be granted overseas.
10. Please explain that privacy overseas may not be the same as New Zealand law.

PK PIS/CF

1. Please state where the blood is being sent for analysis
2. Please amend error in stating that the study doctor is the site selected.
3. Please include a Māori tissue statement (outlined above)

Home Study Visits PIS/CF

1. The Committee noted there is mention of a device, but this is not mentioned elsewhere.
2. Need to state whether you are providing identifiable/confidential information to a third party who will be conducting the home study visit.

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee.
* Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
* Please provide a safety plan addressing the concerns raised by the Committee *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.25).*
* Please supply evidence of ACC-equivalent compensation available to all participants in the event of injury during the study. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 17.1).*
* Please amend the data and tissue management plan *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15 & 14.17).*

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

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| **5** | **Ethics ref:** | **21/STH/76** |
|  | Title: | Melanoma sentinel lymph node biopsy and completion lymph node dissection: The New Zealand experience |
|  | Principal Investigator: | Mr Brandon Adams |
|  | Sponsor: |  |
|  | Clock Start Date: | 01 April 2021 |

Brandon Adams was present by videoconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This study is a retrospective observational study that will collect histological and demographic data (patient age and gender) for patients who have undergone a sentinel lymph node biopsy for melanoma within New Zealand across a 10-year period from between 1/10/2009 to 1/10/2019. This data will be used to ascertain whether or not the New Zealand population is histologically similar to the second Multicentre Selective Lymphadenectomy trial.

Summary of resolved ethical issues

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

1. The Committee asked for the researcher to explain who is going to identify the information required for this study. The researcher responded that histology labs will be contacted and asked to provide information meeting the study criteria as well as accessing notes from the histology report. No further information outside of the laboratory setting will be accessed such as clinician’s notes. Histology notes will be compared to published data, but no databases will be cross-referenced. After discussion, the Committee was assured that clinical outcomes were not being observed.
2. The Committee stated that a waiver of consent for secondary re-use of identifiable health data was not justified in the study documentation. The Committee noted that consenting to the biopsy is not consent for this data to be used in future research. After discussion, the Committee was satisfied that it was impractical to get consent due to large numbers, mortality rates, causing potential upset, and the low risk it does pose to access only the health information and not the tissue.

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 a more comprehensive protocol documenting the aims, objectives and methods clearly is required.
2. The Committee stated a data management plan is required to satisfy the Committee that privacy and confidentiality is protected. Use of the HDEC template is not mandatory but is encouraged to be adapted or used as a guide (<https://ethics.health.govt.nz/updates/new-templates-datatissue-management-plans>)
3. The Committee stated that while less common, Māori data may be used and included so Māori consultation is required.
4. The Committee noted Standard 9.20 that all researchers conducting health research in New Zealand must collect good-quality ethnicity data unless justification for not doing so is provided. The Committee requested that ethnicity data will be collected if it is possible to do so.
5. The Committee requested to see the additional pending peer reviews when they are available.

Decision

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

1. Please address all outstanding ethical issues, providing the information requested by the Committee.
2. Please update the study protocol, taking into account the feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).*
3. Please supply an independent peer review for the current version of the study protocol. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.26).*
4. Please supply a data management plan to ensure the safety and integrity of participant data *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15).*
5. Please supply evidence of Māori consultation to ensure the study is appropriate for a New Zealand context *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 3.7).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Mrs Helen Walker and Associate Professor Mira Harrison-Woolrych

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| **6** | **Ethics ref:** | **21/STH/77** |
|  | Title: | RESPOND PICU RCT |
|  | Principal Investigator: | Dr David Buckley |
|  | Sponsor: |  |
|  | Clock Start Date: | 01 April 2021 |

David Buckley and Shelley Barlow were present by videoconference 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 purpose of this study is to perform a randomised controlled study in children aged >/= 7 days - <16 years old (NZ) requiring inotropic support for septic shock. This is to compare administration of a combination of Vitamin C, Hydrocortisone and Thiamine, to Hydrocortisone alone, and in comparison to standard care. The researchers aim to determine whether metabolic resuscitation leads to faster recovery of shock and organ dysfunction, measured by increased survival without organ dysfunction, whether it decreases long term disability, and investigate the cost effectiveness in comparison to standard care.

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 if all participants will still receive a baseline of standard of care. The researcher clarified proper treatment is not being withheld and study intervention is in addition to, not instead of.
2. The Committee queried why the treatment is only being continued for 72 hours. The researcher responded that benefit is observed in a short period. If patients have recovered sooner, they will be stopped on treatment, and 72 hours is the maximum and will revert to standard of care if no benefit is observed.
3. The Committee queried if the children can provide their own assent upfront. The researcher responded that the condition they are likely to be seen in does not mean this is possible.
4. The Committee queried the recruitment process to establish there is no possible inducement. The researcher responded that the recruitment will not be done by the clinical team and parents will not be approached by the clinical team for recruitment. The Committee was satisfied with this response.

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 asked for justification of having parents filling in questionnaires about themselves. The researcher responded that all questionnaires are for further follow-up down the track that are validated and administered by neuropsychologists. The Committee stated that personal questions being asked of the participants and the parents to not seem clear in the information sheet and stated that parents were active participants. Please ensure the parents have their own participant information sheet and consent form as a separate component to this study.
2. In addition, the Committee queried what would happen if a parent does not want to complete the questionnaires regarding personal information but agrees for their child to take part. The researcher responded that anything the parent completes is included and accepted. The Committee requested to make it clear in the parent information sheet that their child can still take part even if the parent decides not to complete questionnaires about him/herself.
3. The Committee noted that as some participants may turn 16 prior to the follow-up questionnaires being completed, they must have the opportunity to re-consent and agree for the parents to fill in questionnaires on their behalf (or 18 under the Care of Children Act 2004 if they are not well or competent to do so on their own)
4. The Committee asked that since information that is collected about the child from the parent’s responses can be requested to be accessed by the child, because of the nature of the questionnaires, this needs to be stated very clearly in the information sheets and planned for in advance.
5. The Committee requested a summary of where the New Zealand site is deviating from the provided protocol.
6. The Committee stated a data management plan is required to satisfy the Committee that privacy and confidentiality is protected. Use of the HDEC template is not mandatory but is encouraged to be adapted or used as a guide (<https://ethics.health.govt.nz/updates/new-templates-datatissue-management-plans>)
7. The Committee requested written peer review and requested use of the HDEC template to ensure sufficient peer review is provided (<https://ethics.health.govt.nz/guides-templates-forms-0/scientific-peer-review-submissions-%E2%80%93-guidance>)
8. The Committee requested the brochure is amended as it states there are no risks while the participant information sheet outlines risks of participation.
9. The Committee noted that the biobanking in the protocol is not approved as part of this application.

The Committee requested the following changes to the Participant Information Sheet (PIS) and Consent Form (CF):

1. The Parent PIS can be amended to explain that the parent is also a participant, or an additional PIS is required.
2. Page 3 of the parent PIS gives the frequency of drugs for the Metabolic group, but not for the Hydrocortisone only group. While it could be inferred that the frequency of hydrocortisone is the same, this needs to be more clearly outlined.
3. The parent PIS does not explain happens at the end of 72 hours, if the child remains unwell.
4. In the child assent, please explain the child can say NO, even if the parent says YES
5. The parent PIS needs to state that the child will also be asked for their assent and has the right to say no.
6. The Committee noted that participant information must be kept for 10 years following the person turning 16.

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee.
* Please update the study protocol, taking into account the feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).*
* Please supply an independent peer review for the current version of the study protocol. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.26).*
* Please supply a data management plan to ensure the safety and integrity of participant data *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15).*
* Please update the participant information sheet and consent forms, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*

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

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| **7** | **Ethics ref:** | **21/STH/74** |
|  | Title: | HBI-8000-303: HBI-8000 Combined with Nivolumab versus Placebo with Nivolumab in Patients with Unresectable or Metastatic Melanoma |
|  | Principal Investigator: | Dr Gareth Rivalland |
|  | Sponsor: | HUYA Bioscience International, LLC |
|  | Clock Start Date: | 01 April 2021 |

Gareth Rivalland, Amy Tong and John Ning were present by videoconference 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, randomized, double-blind, placebo-controlled Phase 3 study of HBI-8000 or Placebo combined with nivolumab in patients ≥12 years of age with previously untreated metastatic or unresectable melanoma.

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 if participants are likely to be recruited by their treating clinicians and noted their concerns for patients feeling obliged to participate. The researcher responded that the lack of specialists means they are unable to separate the treating clinicians from the research. The normal process is that the patient understand that this is purely voluntary, and the potential participant can take information away to decide and will discuss their participation with a research nurse at a later point. The Committee was satisfied with this response.
2. The Committee queried if participants will be monitored quite closely. The researcher confirmed they are, and an independent data monitoring committee is overseeing the study.
3. The Committee queried the response in the application form that stated Māori consultation was not requested, with a second statement inferring it is being performed. The researcher clarified Māori consultation is being performed.
4. The Committee noted that tissue will be sent overseas to Singapore for analysis and queried if all archival tissue will be used up or returned. The researcher clarified that archival tissue is returned.

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 that there are some significant safety concerns, and more than 10% of people experience low platelet counts. The Committee asked for further information on what proportion of participants have had to withdraw from the study as a result of adverse events.
2. While the required statements about data and privacy have been included in the participant information sheet, the Committee stated a data management plan is required to satisfy the Committee that privacy and confidentiality is protected. Use of the HDEC template is not mandatory but is encouraged to be adapted or used as a guide (<https://ethics.health.govt.nz/updates/new-templates-datatissue-management-plans>)
3. The Committee requested clarification in the insurance certificate as it covers less participants that the application form estimated may be enrolled.
4. The Committee noted that ethnicity data wasn’t being collected for the study which is required in New Zealand unless justification is provided. The Committee requested amendments to the study documentation to ensure good quality ethnicity data is collected at New Zealand sites.

The Committee requested the following changes to the Participant Information Sheet (PIS) and Consent Form (CF):

1. Section 10 under PIS (what are possible risks), please explain further the specific adverse events that have been identified, using bullet points, and providing information on how many people have experienced these in the trials
2. Please include information on what can be done about possible side-effects.
3. Lay-language title required that describes in simple terms what the study is about.
4. Footers require review and amending.
5. Please include a lay-language amended table of assessments.
6. Please review the macrons for Māori words as some are in the incorrect places.
7. Page 9/10 has a formulation statement in the risks section. Please remove.
8. Please review for redundant information.

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee.
* Please supply a data management plan to ensure the safety and integrity of participant data *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15).*
* Please update the participant information sheet and consent forms, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Mrs Helen Walker and Associate Professor Mira Harrison-Woolrych.

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| **8** | **Ethics ref:** | **21/STH/79** |
|  | Title: | EQRx143-101: A study comparing the Pharmacokinetics of EQRx143 in healthy Caucasian and Ethnic Chinese populations. |
|  | Principal Investigator: | Dr Paul Hamilton |
|  | Sponsor: | Novotech (New Zealand) Limited |
|  | Clock Start Date: | 01 April 2021 |

Paul Hamilton and Jessie Kane were present by videoconference 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. EQ143 is being developed for the treatment of cancer. EQ143 is currently approved in China for the treatment of adult patients with advanced Non-small cell lung cancer. The aim of this study is to compare the levels of EQ143 in the blood (pharmacokinetics) between adult healthy Caucasian and Ethnic Chinese populations.

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 if the Future Unspecified Research (FUR) described in the application form is unspecified, as the information sheet outlines only PK research on the drug. The researcher responded that there may be unspecified research in future but currently only PK is known.
2. In the application form, r.3.1.11 states that samples will be destroyed at the end of the study while r.3.7 states mandatory retention for 15 years post study completion. In addition, the participant information sheet states retention of 5 years. The researcher clarified retention is for 5 years.

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 asked the researchers to consult with relevant stakeholders given this study is targeting a particular ethnicity, to ensure study conduct is culturally appropriate.
2. The Committee asked the researchers to check if the insurance can be increased to 10 million as 5 million is considered quite low.

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

1. Include address of global sponsor.
2. Make sure short title is in lay-language.
3. Make sure participants are referred to as such and not subjects.
4. Note that statement that all research is reviewed by HDEC is incorrect.
5. Include the reimbursement rate for backup participants.
6. Contraception requirements on page 12 are inconsistent in terms of female partners vs female participants. Please amend for consistency.
7. Sperm donation is restricted post-dose, however there are no restrictions for egg donation. Provide a justification for this or amend study documentation to restrict egg donation post dose.
8. Collection of pregnancy information should be subject to additional optional consent. Please delete the statement that infers this is mandatory.
9. Remove statement about optional future PK in the main information sheet.
10. Please review for duplicated clauses in consent forms.
11. The participant should have the option of receiving a summary of their results; please provide optional tick-boxes for this.
12. Replace “avoid eating” with “must not eat”.
13. Please revise statement in the optional PISCF about genetics as currently the optional PISCF relates to PK only. If broader future research is intended the document must be re-written to address this.

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee
* Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*

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| **9** | **Ethics ref:** | **21/STH/70** |
|  | Title: | Direct oral anticoagulants for cerebral venous thrombosis |
|  | Principal Investigator: | Dr Teddy WU |
|  | Sponsor: |  |
|  | Clock Start Date: | 25 March 2021 |

Teddy Wu was present by videoconference 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 collaborative international observational study looking at patients with strokes due to clots in the cerebral veins called cerebral venous sinus thrombosis. The aim of this study is to assess the safety and efficacy of direct oral anticoagulants in treating these patients in the real-world setting.

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 that proxy consent is not permitted in New Zealand except under limited circumstances, and best-interests argument and information sheet is not appropriate for this study design. As a result documentation related to best interest / proxy consent is not approved as part of this application.
2. After discussion, the Committee stated that as this is observational research involving the secondary use of routinely collected data only, a justification for waiver of consent for secondary re-use of health information for those who cannot provide consent may be appropriate.
3. The Committee requested either a justification for waiver of consent, or confirmation that only data from participants providing independent informed consent will be included in the study.
4. The Committee stated a data management plan is required to satisfy the Committee that privacy and confidentiality is protected. Use of the HDEC template is not mandatory but is encouraged to be adapted or used as a guide (<https://ethics.health.govt.nz/updates/new-templates-datatissue-management-plans>)

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

1. Please amend references to friend/whanau or ‘you’ for consistency in the main information sheet.
2. Blood sample collection reference should be removed as this is part of standard of care.

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee
* Please supply justification for a waiver of consent for secondary re-use of health information if data that is not consented for is to be included in the study *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.28-12.30).*
* Please supply a data management plan to ensure the safety and integrity of participant data *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15).*
* Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Full Committee (online).

## General business

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

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| **Meeting date:** | 11 May 2021, 10:00 AM |
| **Meeting venue:** | ONLINE - Zoom Meeting |

The following members tendered apologies for this meeting.

1. **Review of 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 2.40pm