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| **Committee:** | Southern Health and Disability Ethics Committee |
| **Meeting date:** | 13 June 2023 |
| **Zoom details:** | 965 0758 9841 |

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| **Time** | **Review Reference** | **Project Title** | **Coordinating Investigator** | **Lead Reviewers** |
| 10:30am-11:00am | 2023 FULL 13807 | ICare-RURAL POC | Dr Rory Miller | Dr Devonie Waaka & Mr Jonathan Darby |
| 11:00am-11:30am | 2023 FULL 16649 | Comparison of two oral rosuvastatin formulations. | Dr Noelyn Hung | Dr Mira Harrison-Woolrych & Mr Dominic Fitchett |
| 11:30pm-12:00pm | 2023 FULL 17925 | MK-0616-017: A Phase 3 Study of MK-0616 in Adults With Heterozygous Familial Hypercholesterolemia | Dr Rosamund Carey | Assoc. Professor Nicola Swain & Ms Dianne Glenn |
| 12:00pm-12:30pm |  | **Break 30 minutes** |  |  |
| 12:30pm-1:00pm | 2023 FULL 17941 | M23-699 SELECT - SLE: Upadacitinib in moderate to severe SLE | Dr Mark Sapsford | Dr Andrea Forde & Mr Dominic Fitchett |
| 1:00pm-1:30pm | 2023 FULL 17954 | Dose ranging study to evaluate the safety and efficacy of tildacerfont in adults with classic Classic Congenital Adrenal Hyperplasia (CAH) (SPR001-203) | Dr Simon Young | Dr Mira Harrison-Woolrych & Ms Dianne Glenn |
| 1:30pm-2:00pm | 2023 FULL 18002 | A safety and efficacy study to evaluate tildacerfont in the reduction of Glucocorticoid Steroid Doses in Adult CAH (SPR001-204) | Dr Simon Young | Dr Andrea Forde & Dr Cordelia Thomas |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Devonie Waaka | Non-lay (Intervention studies) | 13/08/2021 | 12/08/2022 | Present |
| Assc Prof Mira Harrison-Woolrych | Non-lay Intervention/Observational studies) | 28/06/2019 | 28/06/2020 | Present |
| Mr Dominic Fitchett | Lay (the Law) | 05/07/2019 | 05/07/2022 | Present |
| Ms Amy Henry | Non-lay (Observational studies) | 13/08/2021 | 13/08/2024 | Apologies |
| Ascc. Prof Nicola Swain | Non-lay Intervention/Observational studies) | 22/12/2021 | 22/12/2024 | Present |
| Ms Dianne Glenn | Lay (Consumer/Community Perspectives) | 10/07/2022 | 10/07/2025 | Present |
| Ms Neta Tomokino | Lay (Consumer/Community Perspectives) | 10/07/2022 | 10/07/2025 | Apologies |
| Mr Jonathan Darby (Co-opted) | Lay (the Law/Ethical reasoning) | 13/08/2021 | 13/08/2024 | Present |
| Dr Cordelia Thomas (Co-opted) | Lay (the Law) | 22/03/2020 | 22/03/2024 | Present |
| Dr Andrea Forde (Co-opted) | Non-lay Intervention studies) | 13/12/2021 | 13/12/2024 | Present |

## Welcome

The Chair opened the meeting at 10.00am and welcomed Committee members, noting that apologies had been received from Ms Neta Tomokino and Ms Amy Henry. A karakia was performed.   
  
The Chair noted that it would be necessary to co-opt members of other HDECs in accordance with the Standard Operating Procedures. Dr Andrea Forde, Dr Cordelia Thomas and Mr Jonathan Darby confirmed their eligibility and were co-opted by the Chair as a 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 May 2023 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **2023 FULL 13807** |
|  | Title: | ICare-RURAL POC - Improving Care in Rural and URgent care centres for patients with possible Acute coronary syndrome using the Latest Point-of-Care technology |
|  | Principal Investigator: | Dr Rory Miller |
|  | Sponsor: | University of Otago |
|  | Clock Start Date: | 01 June 2023 |

Dr Rory Miller was present via 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 resolved ethical issues

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

1. The Committee noted that the purpose of this project is to assess the implementation of the rollout of a new standard of care pathway and acknowledged the legal opinion provided that this was not research.
2. The Committee raised concerns regarding the lack of consent and to how many participants this may apply. The number of participants was not consistent across the protocol and information sheets. The researcher responded by explaining the current study would only seek to recruit 1400 participants. The adverts provided would be ample in content to give participants the chance to opt-out should they not wish their data to be used. In all cases, current standard of care would be employed. The Committee noted that the request for waiver was sufficiently justified.
3. The Committee noted that the information sheets on site would be utilised in the event of someone requesting more information to reduce the burden for practitioners in the centres.
4. The Committee clarified the presentation of chest pain would not exclude those assigned female at birth given these people tend not to present classically when experiencing a myocardial infarction (MI).

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 requested that the advertisements be updated so as to not mislead participants in terms of what the study may achieve or provide. Please be clear that what is being investigated is the amount of time that people are waiting. Wording to the effect of “may shorten time people need to stay in healthcare centres and reduce resources” would be sufficient. The Committee would like to see the removal of jargon that is not lay-friendly language. This includes terms such as “quality assurance”, “pilot study” etc.

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

1. Please simplify the information to summarise what will happen to participant’s data.
2. Please review for lay language.
3. On page 2, there is mention that this is a “QI project, not a clinical trial or study”. However, later in the document it is referred to as a study. Please consistently refer to it as a project.
4. On page 4, the statement “if you want the results of your screening or safety tests”’ is the first mention of screening/safety tests, please elaborate on these tests before mentioning the return of results.
5. When talking about Māori cultural support, this doesn’t need to be “if you have concerns/complaints”, etc. Please remove this.
6. Please remove the Ethics 0800 number from the contact section as this is no longer active. Please consult the [HDEC PIS template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-v5.0april2023.doc) for updated contact information.

**Decision**

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

* please address all outstanding ethical issues raised by the Committee
* please update the Participant Information Sheet and Consent Form, taking into account the 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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| **2** | **Ethics ref:** | **2023 FULL 16649** |
|  | Title: | A randomised, open-label study to compare the bioavailability of 1 x 6.3 mg rosuvastatin orally disintegrating tablet (ODT) taken  sublingually (Aspen) versus 1 x 10 mg Crestor® oral tablet (Menarini, Australia) in healthy participants under fasting conditions. |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Aspen Pharmacare Australia Pty Ltd |
|  | Clock Start Date: | 01 June 2023 |

Linda Folland and Dr Noelyn Hung were present via 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 resolved ethical issues

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

1. The Committee noted that the request for a closed meeting was not sufficiently justified given the application review would not in any way pose an issue to commercial sensitivity as only the ethical aspects of the study would be discussed. The Committee and the researchers agreed on this and the review continued as part of the open meeting.
2. The Committee noted there will be SCOTT approval before proceeding.

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 requested that the inclusion criteria be extended to 65 years given the drug would mainly be used in real world application by those in the age group of 55-65 years.
2. The Committee noted the additional non-SCOTT peer review was not attached to the application. Please provide this if this study does not go for full SCOTT review.
3. The Committee requested a revision of the advertisements to be more lay friendly and remove the mention of “generic formulation”.
4. The Committee requested that this trial be registered with an appropriate WHO approved clinical trial registry.
5. The Committee noted the mention in several parts of the application form and participant information sheet that it is anticipated the test product will reduce the instance of myalgia, but nowhere in the protocol or application form was the scientific basis for this hypothesis outlined. The Committee requested this be addressed in study documentation.

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

1. Please clarify that the reference product is approved for use in New Zealand, but that the test product is not. Please also clarify that the formulation is an investigational product.
2. As a secondary aim of the study is to compare possible adverse effects, please delete information stating that myalgia may be lower in the test formulation. This may influence reporting of adverse events by participants, particularly as the study is open label.
3. Please use the [HDEC reproductive risks template](https://ethics.health.govt.nz/guides-templates-and-forms/participant-information-sheet-templates/) information regarding male contraception as this is not well explained or explicit enough.
4. Please state that only women of child-bearing potential, who require pregnancy tests during the study, will receive the higher reimbursement amount.
5. Please specify the time of day for admission into the unit rather than “12 hours before dosing”.
6. Please amend the statement regarding fasting to make it clear that participants are advised to eat a substantial meal prior to admission to the unit, as they will not receive any food from the time of admission until after 4 hours after dosing.
7. Please extend the sentence around the exclusion of those with Asian heritage to explain in lay language the impact of their inclusion, such as complicating the interpretation of study results.

**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 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).*
3. 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*).

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

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| **3** | **Ethics ref:** | **2023 FULL 17925** |
|  | Title: | MK-0616-017: A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of MK-0616 in  Adults With Heterozygous Familial Hypercholesterolemia |
|  | Principal Investigator: | Dr Rosamund Carey |
|  | Sponsor: | Merck Sharp & Dohme (New Zealand) Ltd |
|  | Clock Start Date: | 01 June 2023 |

Dr Rosamund Carey, Frances Rosario, Kim Huljich and Dr Mike Williams was present via 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 resolved ethical issues

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

1. The Committee clarified that all participants would be established on lipid lowering therapy prior to being screened for the study.
2. The Committee clarified the training and experience of the Coordinating Investigator (CI), noting that no previous experience as a site Principal Investigator (PI) and only a few years’ clinical research experience was listed in the CI’s curriculum vitae (CV). The Committee further noted that the CI did not appear to be taking an active role in the discussion of the application, with most questions responded to by Dr Williams. Dr Carey clarified that she had extensive clinical trial experience in South Africa over many years, which were not included in the submitted CV, and was currently the site PI for a clinical trial. The Committee asked whether Dr Carey had any specialist training in the disease area under study. Dr Williams stated that Dr Carey had extensive experience as a GP and as such managed people with the condition under study routinely. It was also clarified that as she was not experienced with ethics application in New Zealand, Dr Williams was mentoring her through the HDEC process and would continue to act as a CI mentor throughout the trial.

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 requested the provision of any advertising material that may be used.
2. The Committee noted that the study must be registered with a WHO-approved clinical trials registry prior to starting.
3. The Committee requested that the researcher clarify whether the genetic testing prior to the study commencement will be a part of the study in New Zealand.
4. The Committee queried the length of the placebo period, given that injectable medicines in the same class are approved for use overseas. The Committee requested the Sponsor consider undertaking an interim analysis after 26 weeks of treatment. The Committee requested that a justification be provided should this not be deemed possible, given it could be unethical to continue the placebo arm if there was benefit determined in the group on active treatment.
5. The Committee questioned how the optional genetic testing result would be fed back to the participant, as the CI did not have experience in this area. The Committee requested that a process be put in place to ensure appropriate advice and follow-up, for example with a clinical geneticist.
6. F9.1 of the application form states the limited screening sample will be “performed at a local laboratory (and) ... destroyed according to local procedure following analysis’; the participant information sheet (PIS) states it will be sent to a central laboratory. Please clarify what is intended and correct either the application form or PIS.
7. The Committee noted that the amount of reimbursement provided to participants should be consistent across all New Zealand sites, to ensure participants are treated fairly. Please confirm that reimbursement will be the same for all New Zealand participants or provide a justification for the differential rate.
8. The Committee requested the following changes to the Data and Tissue Management Plan (DTMP):
   1. Please remove reference to including month of birth with de-identified data; this should be year of birth only.
   2. Section 12.2 of the DTMP states that participants will not be informed of the results of optional genetic testing for HeFH; the PIS states participants will be informed. Please clarify what is intended and correct information accordingly.

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

All:

1. Please amend the sentence around potential eligibility to participate despite not needing additional cholesterol-lowering treatment, as the sentence currently reads as though participants on no lipid-lowering therapy may be enrolled.
2. Please remove duplicated headings.
3. Please specify that there are no reproductive risks for male participants or their partners of child-bearing potential.
4. Please clarify on page 14 that the sponsor may only transfer coded health data to other countries.
5. Please correct the statement noting that notifiable diseases are reported to the Ministry of Health. This is incorrect and should read that they will be reported to the Medical Officer of Health. Please also clarify that the statement relates to Hepatitis B and C.
6. Please amend the amount of blood collected to read in millilitres not in tablespoons or teaspoons.
7. All PIS/CF currently state at the end “if you need an INTERPRETER please tell us”, this should be at the beginning of each PIS.

Screening PIS/CF:

1. Please ensure that information pertaining to the sending or destruction of tissue is consistent and accurate.

Genetic Testing PIS/CF:

1. Please tidy up this document.
2. Please clarify the potential consequences of receiving this genetic testing, including whether the results of the test may have significant implications for the participant's blood relatives.
3. Please clarify what follow-up will be offered to participants with a confirmed genetic basis for their HeFH. In particular, clarify whether external specialist follow-up will be arranged.
4. Please clarify whether the results of the test may affect the participant's (or blood relatives’) ability to obtain health insurance.

**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 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).*
3. 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*).

After receipt of the information requested by the Committee, a final decision on the application will be made by Associate Professor Nicola Swain and Ms Dianne Glenn.

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| **4** | **Ethics ref:** | **2023 FULL 17941** |
|  | Title: | A Phase 3 Program to Evaluate the Safety and Efficacy of Upadacitinib in Subjects with Moderately to Severely Active Systemic Lupus Erythematosus. |
|  | Principal Investigator: | Dr Mark Sapsford |
|  | Sponsor: | Abbvie Ltd |
|  | Clock Start Date: | 01 June 2023 |

Dr Mark Sapsford and Esther Ji were present via 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 resolved ethical issues

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

1. The Researchers adequately justified the rationale for excluding certain population ages.
2. The Committee clarified that all Quality of Life (QOL) surveys had been validated.

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 upadacitinib is an approved medicine being trialled for a new indication, so would not be subject to SCOTT review. Please instead submit an independent scientific peer review by a suitably qualified expert in the field.
2. The Committee noted referral to psychiatrists for mental health issues is tricky in NZ. Please review this referral pathway to be more accessible and accurate for the New Zealand healthcare system.
3. The Committee noted that one of the Investigator’s Brochures (IBs) had not been provided. The researcher explained that one of the IBs was currently being revised and would be made available once finished.
4. The Committee noted that the amount for reimbursement was low for the duration and risk associated with a clinical trial.
5. Under return of results, it is stated that participants cannot request results of safety assessments while on the study. Please clarify why participants cannot request copies of safety assessments while on-study. Participants routinely request this information to prevent having to repeat tests required for standard care.
6. If Case Report Form (CRF)-specified ethnicity/race groups are not reflective of the New Zealand population, please make sure that site-level ethnicity data is collected using New Zealand ethnicities.
7. The Committee requested the following changes to the Data and Tissue Management Plan (DTMP):
   1. Please remove the blue text note to researchers on page 3.
   2. Section 5.1 states that participants will be informed of a privacy breach only if it is judged notifiable. HDEC's expectation is that affected participants are informed of any privacy breach unless there are valid reasons for not doing so. Please amend Section 5.1 to reflect this.
   3. Please amend Section 7.5 to address optional future uses of tissue; the current description is for data use only.
   4. Section 12 states that 'If the participant withdraws permission to participate in follow up or withdraws permission for collection of personal information, a limited amount of new personal information may still be collected including safety information that may be related to the participant’s participation in the study...'. Please clarify how the collection of new information against the participant's wishes is ethically justified.

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

Main PIS/CF:

1. Please review for repeated information.
2. Please remove cup measurements for blood volumes.
3. Please state that karakia will not be available at time of tissue destruction.
4. Please remove reference to SCOTT review.
5. Please amend reference to the study drug being an “experimental drug”; it is an approved drug being used for a new indication.
6. Please move the consent for home delivery to be with the rest of the consent form.
7. Please amend “please update the study doctor” to “please inform the study doctor”
8. Please state that tuberculosis may also require reporting to the Medical Officer of Health.
9. Anaemia due to blood collection is not expected given the total blood volume required during the study. Please delete this as a study risk.
10. It is assumed that the $100 reimbursement referenced is per visit, not for the entire study. It is also noted that reimbursement is paid 'periodically’, which is very vague; participants should be reimbursed promptly for study-related expenses. Please clarify what is intended and amend accordingly on page 18.
11. Please clarify that collection of pregnancy outcome data will be subject to the participant providing optional additional consent on page 24.
12. Please amend the statement on page 24 reading “may have a right” as participants *do* have the right, please amend this to read “you have the right”.
13. Please include an optional tick box for participants to indicate whether they wish to receive a lay summary of the study results in the consent form.
14. Please note that the current reproductive risks section is outdated and inaccurate, please refer to the [HDEC template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-v5.0april2023.doc) for an accurate statement.
15. Please remove the signing space in the consent form for legally authorised representative as this is not permitted in New Zealand.

Future Research PIS/CF:

1. Please remove cup measurements for blood volumes on page 2.
2. Please explain the significance of samples being analysed at non-GLP laboratories on page 3.
3. On page 4 it is stated that “if you withdraw…. They will discuss health risks”. Given that there is no extra risk this should be removed.

**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 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).*
3. 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*).

After receipt of the information requested by the Committee, a final decision on the application will be made by Mr Dominic Fitchett and Dr Andrea Forde.

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| **5** | **Ethics ref:** | **2023 FULL 17954** |
|  | Title: | A Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study to Evaluate the Efficacy and Safety of SPR001 (Tildacerfont)  in Adult Subjects with Classic Congenital Adrenal Hyperplasia (SPR001-203) |
|  | Principal Investigator: | Dr Simon Young |
|  | Sponsor: | Spruce Biosciences, Inc |
|  | Clock Start Date: | 01 June 2023 |

No one from the research team was present via 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 outstanding ethical issues

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

1. In a long-term efficacy study it would be expected that there is a potential for individual benefit. The Committee requested clarification as to why no therapeutic benefit is intended, as stated in B1 of the application form.
2. The Committee requested clarification as to whether investigators at either site may also provide specialist clinical care to potential participants.
3. The Committee requested that New Zealand sites collect ethnicity data relevant to the New Zealand population. This may need to be collected in addition to CRF-specified race/ethnicity fields.
4. The Committee noted that the text in the yellow box in the CAHBOOK states that there is an equal chance of being placed on placebo. This is not true as randomisation is 1:1:1:1, please correct to prevent any participants from being misled.
5. The Committee requested that the food amounts in the CAHBOOK be converted from ounces to grams as most New Zealanders are not familiar with the former.
6. The Committee suggested that the CAHFAQ should note New Zealand site participation in the trial.
7. The Committee requested that the researcher deletes 'Harmful consequences of excessive, lifelong glucocorticoid use' from the advertisement, as this is contrary to HDEC advertising guidance that language that 'plays on fear should not be used'.
8. The Committee requested an amended Sponsor Certificate of Insurance specifying New Zealand as territory.
9. The Committee noted that the potential for hepatotoxicity or abnormal thyroid function tests is discussed in the protocol and IB. Please confirm the expected turn-around time of the central lab in reporting safety labs back to New Zealand sites and clarify whether this is considered sufficient to adequately monitor safety.
10. The Committee requested a summary of the commonly described or potentially serious adverse effects of the study drug; it is expected that these would be noted in E.1 of the application form.
11. The Committee noted that Sponsor authorisation is required due to the previous application being declined, resulting in changes to the application form and submitted documentation. Please amend the form and ensure Sponsor Authorisation is obtained for this submission.
12. The Committee requested clarification as to whether the study drug would be provided should clinical benefit be derived from its use even after the trial has ended or the drug does not become funded in New Zealand.
13. The Committee requested the following changes to the Data and Tissue Management Plan (DTMP):
    1. Please resolve inconsistencies regarding the use of data and tissue banks (Sections 8.2, 87 and 8.8).
    2. Please resolve inconsistencies regarding the use of New Zealand laboratories (Sections 7.2 and 10.1).
    3. Section 8.4 states anonymised data will be sent overseas; please amend to reflect that data is de-identified.
    4. Section 8.5 does not state future use of tissue is optional and allows unspecified unrelated research. Please amend to clearly describe what future research will be conducted on tissue, and whether this is mandatory or optional.
    5. Section 10.2.1 states mandatory tissue samples will be 'retained for up to 25 years then destroyed by shredding'. Please amend method of destruction and maximum retention period (application form states 5 years).
    6. Please clarify what genetic results of clinical significance could occur during the trial (Section 12.1).
    7. The appendix PDF does not open. Please append the document.
    8. Please note that full date of birth is an indirect identifier and should not be included with de-identified data as was mentioned in the application form.
    9. Please clarify whether karakia will be made available at the time of tissue destruction.
    10. Please review for formatting and align headings and subheadings.
    11. Please clarify the collection and storage of data for the courier of the study treatments and how this will be managed and justify the reason for this data to be collected and kept.

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

Main PIS/CF:

1. Please note a simple lay title is required as the main title of the PIS/CF.
2. Please review to ensure the same font is used throughout to improve readability.
3. Please delete 'If you choose to withdraw before the planned final visit, you will be asked to complete as many of the originally intended study visits as you are willing to complete'. This is contrary to the concept of being free to withdraw from the study at any time.
4. Please state approximate number of New Zealand participants on page 2.
5. Please delete teaspoon and cup measurements of blood volume and replace with millilitres from page 5 onwards.
6. Please explain the optional genetic testing in more detail. This should provide a lay explanation of what genes and DNA are, whether the participant's entire genetic code will be sequenced / recorded, whether 'future genetic testing' will be limited to genetic testing related to drug or disorder under study, and whether there is a risk of genetic results being matches across databases (e.g. law enforcement or commercial ancestry databases). Please explain also whether clinically significant incidental findings may arise; whether these could be clinically actionable; and the options available to participants in terms of being informed of such results.
7. Please address the potential risks on page 12, of thyroid function changes and testicular changes have not been discussed.
8. Please simplify the contraceptive section, using lay terms and examples widely recognised in New Zealand. Use of the [HDEC reproductive risks template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-reproductive-risks-v.4.0-april2023.docx) is encouraged.
9. Collection of pregnancy outcome data for pregnant participants requires additional optional consent. Please amend the information on page 14 accordingly.
10. Please remove 'with your consent' from the statement regarding General Practitioner (GP) notification on page 16; this is a mandatory component of study participation.
11. Please amend the Medical Officer of Health statement, which currently includes 'enter those tests applicable to your study' on page 16.
12. Please delete optional tick boxes for withdrawal of data and GP notification on the consent form; these are mandatory.
13. The consent clause about not informing participants of incidental findings is problematic, given that GP notification of these is mandatory. No distinction is made between clinically actionable and non-actionable findings, or whether this relates to all results or only the genetic research. Either provide much more clarity in the body the PIS or explain that participants will be informed of any abnormal findings that may be important for their health I page 21.
14. Please clarify whether the discussion with a GP will be paid for by the trial.
15. Please rephrase the statement around the notification of suicidality to a GP. This reads as quite threatening and may create a situation in which participants lie in order to stay in the trial.

Pre-screening PIS/CF:

1. Please state whether pre-screening is a mandatory if the participant wishes to progress to the main study, or whether the blood tests can be collected during the main screening period.
2. Please clarify that satisfactory results in pre-screening do not mean the participant is eligible for the main study (they must also meet study requirement for a number of other screening assessments).
3. Please delete consent clauses not relevant to pre-screening.
4. Please delete optional tick boxes where consent is mandatory.
5. Please include a cultural statement.

**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 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).*
3. 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*).

After receipt of the information requested by the Committee, a final decision on the application will be made by Dr Mira Harrison-Woolrych and Ms Dianne Glenn.

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| **6** | **Ethics ref:** | **2023 FULL 18002** |
|  | Title: | Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of SPR001 (Tildacerfont) in Reducing Supraphysiologic Glucocorticoid Use in Adult Subjects with Classic Congenital Adrenal Hyperplasia (SPR001-204) |
|  | Principal Investigator: | Dr Simon Young |
|  | Sponsor: | Spruce Biosciences, Inc |
|  | Clock Start Date: | 01 June 2023 |

No one from the research team was present via 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 outstanding ethical issues

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

1. In a long-term efficacy study it would be expected that there is a potential for individual benefit. The Committee requested clarification as to why no therapeutic benefit is intended.
2. The Committee requested clarification at to whether investigators at either site may also provide specialist clinical care to potential participants.
3. The Committee requested that New Zealand sites collect ethnicity data relevant to the New Zealand population. This may need to be collected in addition to CRF-specified race/ethnicity fields.
4. The Committee requested that the food amounts in the CAHBOOK be converted from ounces to grams as most New Zealanders are not familiar with the former.
5. The Committee suggested that the CAHFAQ should note New Zealand site participation in the trial.
6. The Committee requested that the researcher deletes 'Harmful consequences of excessive, lifelong glucocorticoid use' from the advertisement. As this is contrary to HDEC advertising guidance that language that 'plays on fear should not be used'.
7. The Committee requested an amended Sponsor Certificate of Insurance specifying New Zealand as territory.
8. The Committee noted that the potential for hepatotoxicity or abnormal thyroid function tests is discussed in the protocol and IB. Please confirm the expected turn-around time of the central lab in reporting safety labs back to New Zealand sites and clarify whether this is considered sufficient to adequately monitor safety.
9. The Committee requested a summary of the commonly described or potentially serious adverse effects of the study drug; it is expected that these would be noted in E.1 of the application form.
10. The Committee noted that Sponsor authorisation is required due to the previous application being declined, resulting in changes to the application form and submitted documentation. Please amend the form and ensure Sponsor Authorisation is obtained for this submission.
11. The Committee requested clarification as to whether the study drug would be provided should clinical benefit be derived from its use even after the trial has ended or the drug does not become funded in New Zealand.
12. The Committee requested the following changes to the Data and Tissue Management Plan (DTMP):
    1. Please resolve inconsistencies regarding the use of data and tissue banks (Sections 8.2, 87 and 8.8).
    2. Please resolve inconsistencies regarding the use of New Zealand laboratories (Sections 7.2 and 10.1).
    3. Section 8.4 states anonymised data will be sent overseas; please amend to reflect that data is de-identified.
    4. Section 8.5 does not state future use of tissue is optional and allows unspecified unrelated research. Please amend to clearly describe what future research will be conducted on tissue, and whether this is mandatory or optional.
    5. Section 10.2.1 states mandatory tissue samples will be 'retained for up to 25 years then destroyed by shredding'. Please amend method of destruction and maximum retention period (application form states 5 years).
    6. Please clarify what genetic results of clinical significance could occur during the trial (Section 12.1).
    7. The appendix PDF does not open. Please append the document.
    8. Please note that full date of birth is an indirect identifier and should not be included with de-identified data as was mentioned in the application form.
    9. Please clarify whether karakia will be made available at the time of tissue destruction.
    10. Please review for formatting and align headings and subheadings.
    11. Please clarify the collection and storage of data for the courier of the study treatments and how this will be managed and justify the reason for this data to be collected and kept.

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

Main PIS/CF:

1. Please note a simple lay title is required as the main title of the PIS/CF.
2. Please review to ensure the same font is used throughout to improve readability.
3. Please delete 'If you choose to withdraw before the planned final visit, you will be asked to complete as many of the originally intended study visits as you are willing to complete'. This is contrary to the concept of being free to withdraw from the study at any time.
4. Please state approximate number of NZ participants on page 2.
5. Please delete teaspoon and cup measurements of blood volume and replace with millilitres from page 5 onwards.
6. Please explain the optional genetic testing in more detail. This should provide a lay explanation of what genes and DNA are, whether the participant's entire genetic code will be sequenced / recorded, whether 'future genetic testing' will be limited to genetic testing related to drug or disorder under study, and whether there is a risk of genetic results being matches across databases (e.g. law enforcement or commercial ancestry databases). Please explain also whether clinically significant incidental findings may arise; whether these could be clinically actionable; and the options available to participants in terms of being informed of such results.
7. Please address the potential risks on page 12, of thyroid function changes and testicular changes have not been discussed.
8. Please simplify the contraceptive section, using lay terms and examples widely recognised in NZ. Use of the [HDEC reproductive risks template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-reproductive-risks-v.4.0-april2023.docx) is encouraged.
9. Collection of pregnancy outcome data for pregnant participants requires additional optional consent. Please amend the information on page 14 accordingly.
10. Please remove 'with your consent' from the statement regarding General Practitioner (GP) notification on page 16; this is a mandatory component of study participation.
11. Please amend the Medical Officer of Health statement, which currently includes 'enter those tests applicable to your study' on page 16.
12. Please delete optional tick boxes for withdrawal of data and GP notification on the consent form; these are mandatory.
13. The consent clause about not informing participants of incidental findings is problematic, given that GP notification of these is mandatory. No distinction is made between clinically actionable and non-actionable findings, or whether this relates to all results or only the genetic research. Either provide much more clarity in the body the PIS or explain that participants will be informed of any abnormal findings that may be important for their health I page 21.
14. Please clarify whether the discussion with a GP will be paid for by the trial.
15. Please rephrase the statement around the notification of suicidality to a GP. This reads as quite threatening and may create a situation in which participants lie in order to stay in the trial.
16. Please rephrase the request for participants to take a meal that is less than 50% fat. This should be in lay terms.

Pre-screening PIS/CF:

1. Please state whether pre-screening is a mandatory if the participant wishes to progress to the main study, or whether the blood tests can be collected during the main screening period.
2. Please clarify that satisfactory results in pre-screening do not mean the participant is eligible for the main study (they must also meet study requirement for a number of other screening assessments).
3. Please delete consent clauses not relevant to pre-screening.
4. Please delete optional tick boxes where consent is mandatory.
5. Please include a cultural statement.

**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 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).*
3. 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*).

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

## General business

1. The Chair reminded the Committee of the date and time of its next scheduled meeting:

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| **Meeting date:** | 11th July 2023 |
| **Zoom details:** | To be determined |

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.

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

The meeting closed at 1.50pm.