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| **Committee:** | Southern Health and Disability Ethics Committee |
| **Meeting date:** | 11 February 2020 |
| **Meeting venue:** | Sudima Hotel, Christchurch Airport, 550 Memorial Drive, Christchurch |

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| **Time** | **Item of business** |
| 11:30am | Welcome |
| 11:35am | Confirmation of minutes of meeting of 10 December 2019 |
| 11:40am   11:45am | General business   * Noting section   New applications (see over for details) |
| 11:45 – 12:10pm  12:10 – 12:35  12:35 – 1:00  1:00 – 1:25  1:25 – 1:50  1:50 – 2:15  2:15 – 2:40 | i 20/STH/28  ii 20/STH/19  iii 20/STH/17  iv 20/STH/13  v 20/STH/18  vi 20/STH/20  vii 20/STH/1 |
| 3:05pm | Meeting ends |

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

## Welcome

The Chair opened the meeting at 11:45am and welcomed Committee members.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

## Confirmation of previous minutes

The minutes of the meeting of 10 December were confirmed.

## New applications

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| **1** | **Ethics ref:** | **20/STH/28** |
|  | Title: | A study of the Efficacy and Safety of Guselkumab inParticipants with Moderately to Severely Active Crohn's Disease Study to evaluate the safety and effectiveness of guselkumab - GALAXI 2 and 3 (Pha |
|  | Principal Investigator: | Prof Michael Schultz |
|  | Sponsor: | Janssen-Cilag (New Zealand) Limited |
|  | Clock Start Date: | 20 February 2020 |

Juliana Suzuki and Dr James Brooker were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This application relates to two randomised Phase 3 active/placebo-controlled superiority trials of guselkumab in severe Crohn's Disease.
2. The study was initially submitted two years ago to HDEC and SCOTT as an umbrella group of trials (one phase 2 trial and two Phase 3 trials). The application was declined twice by HDEC. Eventually the Phase 2 trial (GALAXI I) was approved in isolation by HDEC and SCOTT, with clear direction that the Phase 3 trials (GALAXI II and GALAXI III) would require new applications to each reviewing body.

Summary of resolved ethical issues

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

1. The Committee stated that, contrary to the response given in the application form, screening assessments could reveal incidental findings of clinical significance. The Researchers were asked how these findings will be managed, and they stated that participants will be followed up closely with SOC procedures, and incidental findings would be managed by Dr Schultz, referred to a specialist, and the GP would be informed.
2. The Committee noted that in answer to question p.4.4 it was stated that the study involves kaupapa Maori methodologies, which is incorrect.

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 initial MEDSAFE approval was valid only for GALAXI I, and stated that a new SCOTT application would be needed for GALAXI II and GALAXI III. The Committee noted that the document evidencing peer review was an approved *amendment* to SCOTT. Further, the text in the Post Approval Form referred to documentation regarding urgent safety measures, with no reference to the fact that approval was being sought for GALAXI II and III. The Committee was therefore concerned that SCOTT may have approved the amendment without being aware that SCOTT approval was only in place for the GALAXI I study.

The Researchers asserted that approval for the phase 3 studies had been given, and was evidenced by emails dated December 12 and 13. However, the Committee again noted that the email correspondence referred to was an amendment rather than the new application originally required by SCOTT. The information provided to Medsafe further did not make it clear that the dosing decision memos included with the amendment were for two studies that had not previously been approved by SCOTT.

The Committee requested that the researchers provide Medsafe with the original GALAXI I approval letter (stating that a subsequent application would need to be submitted for the Phase 3 studies). The Committee requested a letter from Medsafe confirming that SCOTT had reviewed and approved the Phase 3 studies as a new application.

1. In reference to the Researcher’s answer to application question R.1.1 (risks associated with the study procedures), the Committee stated that this should address the risks associated with the investigational product, including a summary of the associated risks.  
   The Committee noted that an episode of toxic hepatitis has been associated with the investigational product, and asked if lower doses were intended in the Phase 3 studies than that associated with the event of toxic hepatitis. The researchers were unable to provide any information about dose level or the event of toxic hepatitis.
2. The Committee stated that the Researcher’s answer to application question f.3.2 does not address equipoise. The researcher was asked if there is equipoise, given that ustekinumab has established safety and efficacy in Chron’s Disease, and given that there is a placebo arm. This Committee asked for this to be addressed and for a justification to be given for the inclusion of a placebo arm in addition to active control. The researcher was unable to address this question.
3. The Committee noted that, in the event of a participant withdrawing from the study, the participant’s tissue will not be withdrawn from further analysis unless that is specifically requested.

Research should be designed so as to make withdrawal from the study as easy as possible. Please confirm that participants will be specifically asked if they wish for their tissue to be withdrawn, in the event of withdrawal from the study.

The Committee identified the following issues with the Main Participant Information Sheet and Consent Form and requested the document be amended accordingly:

1. The sentence 'this research study is the first study to use guselkumab in people' is not correct. Please reference GALAXI I and the number of people exposed to the drug (and doses used) in that study.
2. Please state whether the approved dose range for psoriasis is the same as that which will be used in the current study.
3. Please provide more information about the case of toxic hepatitis, and about other adverse liver effects.
4. The PIS states “women must use a highly effective form of contraception”, yet goes on to recommend barrier methods and abstinence, which are not highly effective. Please amend accordingly.
5. The application form states that “samples will be stored securely in the USA but may be relocated at any time”. The Researchers stated that they also have laboratories in Singapore. Please state all known locations clearly in the PIS and explain that the statement ‘may be relocated at any time’ means that samples could be sent anywhere in the world.

A number of other outstanding issues had been identified by Committee members prior to the meeting with regards the submitted PISCF documents (Main, Sub-study, Genetic, Future Unspecified Research and Pregnancy Authorisation Form); surveys; and other submitted material. Due to the decision being made to decline on the basis of the following points, these issues were not raised with the Researchers at the meeting.

Decision

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

* Peer review must deliver an informed opinion. On the basis of the documentation submitted, the Committee was not reassured that SCOTT had been informed about all relevant aspects of the GALAXI phase 2 and 3 studies (*National Ethics Standards* para *9.32*).
* Informed consent requires that participants are informed of the nature, likelihood and severity of all relevant harms (*National Ethics Standards* table *7-1*).
* Researchers should design the study to meet the equipoise standard. Given the established safety and efficacy of ustekinumab, the Committee was not assured that the inclusion of a placebo arm met this standard (*National Ethics Standards* para *10.18*).
* Before conducting research, researchers must develop and record a plan for how they will handle incidental findings (*National Ethics Standards* para *11.48*).

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| **2** | **Ethics ref:** | **20/STH/19** |
|  | Title: | SELECT 2 |
|  | Principal Investigator: | Dr Teddy WU |
|  | Sponsor: | The University of Texas Health Science Center |
|  | Clock Start Date: | 30 January 2020 |

Dr Teddy Wu was present in person for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

The study compares the treatment outcomes for people with clots causing a significant area of ischaemic stroke. The design is a randomised control trial where one group is treated with clot retrieval and medical management and a second group medical management only. Outcomes are measured over 90 days with weekly monitoring post-discharge from hospital. All participants are acutely unwell and are enrolled within 24 hours post-stroke, mostly in Emergency departments. The target population will include those who are unable to give full and informed consent.

Clot retrieval is not currently offered for the proposed study population, as it is not efficacious for all patients, however previous studies indicate that a sub-group of patients may benefit from treatment.

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 whether clot retrieval is already being used in low-risk patients. The Researcher explained that there are two main image-selection techniques being used: a CT scan and perfusion testing. Following those assessments clot retrieval is current SOC in patients with a lower volume of damaged tissue than that considered in this study.

The Committee asked how these procedures are explained to participants, and the Researcher stated that it is explained with a diagram/picture. If, as a consequence of their stroke, the participant does not understand it, then their family is asked if they believe it to be in the patient’s best interests.

1. The Committee asked if there is a risk of patients being worse off from the procedure. The Researcher explained that there is not, as the prognosis is very poor without the procedure.
2. The Committee noted that a device manufacturer is providing the funding for the study, and asked for clarification of the extent of their involvement in the study. The Researcher explained that the manufacturer is not involved in the design or analysis, but will have access to de-identified data at the end of the trial. Stryker Neurovascular is the manufacturer of one of the clot retrieval devices used in this study, but the protocol does not stipulate that the Stryker device must be used.   
   The Committee was satisfied that the manufacturer is not directly benefiting from the study, and that participants injured in the study would be eligible for funding from ACC.
3. The Committee asked why data from the study will not be made available for future research.

The researcher stated that the data set could potentially be made available to other approved researchers in the future, in a de-identified form.

1. The Committee noted that the primary ethical issue in the study is participants’ consent, and that if participants cannot consent, the treatment must be believed to be in their best interests. It stated that the ‘friends and family’ agreement form does not make clear if proxy consent or an expression of the participants’ interests is being sought. It further asked what proportion of patients would typically be unable to give consent.

The Researcher explained that around 50% of patients will not be able to consent and stated that the form is only seeking an expression of whether they believe the patient would wish to participate in the study. The decision as to whether trial participation was in the participant’s best interest would be made by an appropriately qualified clinician.

Summary of outstanding ethical issues

The Committee identified the following issues with the Participant Information Sheet and Consent Form and requested the document be amended accordingly:

1. The Committee expressed concern that most patients would not understand a lot of the information in the main PIS. Please reduce jargon and simplify the title of the PIS.
2. To ensure that the signatory knows that only an opinion as to the participant’s interests is being sought (rather than proxy consent), please make this very clear on the consent form.
3. Please add percentage numbers to the risks section of the PISCF, where available.

Decision

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

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

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

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| **3** | **Ethics ref:** | **20/STH/17** |
|  | Title: | Phase 1/2 study of IMC-I109V in non-cirrhotic HBeAg-negative chronic HBV infection |
|  | Principal Investigator: | Prof Edward Gane |
|  | Sponsor: | Novotech (New Zealand) Limited |
|  | Clock Start Date: | 23 January 2020 |

Prof Edward Gane was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The study investigates a new immune treatment for hepatitis B virus (HBV) infection. This is a first in human, two-part (single ascending dose and multiple ascending dose) study. The safety, antiviral activity and pharmacokinetics of IMC-I109V will be evaluated in adults with non-cirrhotic HBeAg-negative chronic HBV infection.
2. Due to the way IMC-I109V works, all participants in the study must be HLA-A\*02:01 positive. This will be tested for at pre-screening, as it expected only about 10% of the New Zealand target population will carry this genetic variation compared with rates of approximately 50% in some other countries.

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 no animal studies had been conducted due to the human-specific target. The Researcher confirmed that SCOTT approval would be obtained prior to commencing the study.
2. The Committee asked why an internal DSMC was being used, rather than an external DSMC. The Committee expressed concern about the multi-national, multi-centre nature of the trial. The Researcher explained that it is internal as it is a first in human study, and that all Investigators would be involved in dose escalation decisions.

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 a justification of the lack of a placebo arm, as placebo is commonly used in SAD / MAD studies to address potential bias in adverse event reporting.
2. The Committee stated that the insurance certificate has not been provided for review and asked that this be submitted.
3. The Committee questioned the justification for mandatory tissue samples being stored for 15 years after study completion, and asked that this be amended.

The Committee identified the following issues with the Pre-Screening Information Sheet and Consent Form and requested the document be amended accordingly:

1. The pre-screening PIS includes a lot of unnecessary information, particularly for those who are subsequently found to be ineligible for the study. The Committee suggested that a much more abbreviated PIS be developed for pre-screening, with the main study PIS offered to participants who wanted information about the main study at the pre-screening stage.

The Committee identified the following issues with the Main Participant Information Sheet and Consent Form and requested the document be amended accordingly (page numbers provided are for the SAD PISCF, though points also apply to the MAD PISCF):

1. General: please amend the names of the two part of the study to something less emotive than “SAD” and “MAD”. “Single Dose” and “Multiple Dose” is suggested.
2. Page 3 states that all health research in NZ is reviewed by an HDEC. Please delete this sentence, as it is incorrect.
3. Page 3 : Description of study parts is technical (5 - 9 ascending dose cohorts). Please re-write in lay language.
4. Page 4.: The description of study duration is confusing. Week 36 appears to be a typo. Please review and amend where indicated.
5. Page 5: Are radiotherapy and surgery treatment for HBV, or is this a carry-over from another study? Please review and amend as indicated.
6. Page 6: Please simplify the table and make more legible for a lay reader. The table also appears to omit the in-house stay. Please review and amend as indicated.
7. Page 6. The phrases ‘PBMC sample’, ‘PAXgene whole blood mRNA sample’ and 'measure certain biomarkers for exploratory analysis' are meaningless to lay people. Please re-write in lay terms.
8. Page 8: Please state that reimbursement for travel is up to $100 per visit (the text currently makes this appear to be a cumulative figure).
9. Page 8: Please state that the study drug has not been tested in humans or animals.
10. Page 9: Please replace 'oncology' with 'cancer'.
11. Page 9: Please state if there have been serious / severe / fatal infusion reactions or cytokine release syndromes with related drugs. The text appears to underplay the potential seriousness of these reactions.
12. Page 9: Lymphopenia and attendant risk of infection is noted as a risk in the IB but not in the PISCF. Please amend accordingly.
13. Page 13: Should a participant withdraw from the study, please ensure he or she is explicitly asked whether he/she also wishes to withdraw remaining tissue samples.
14. Page 15: Please make it clear that auditors will have access to identifiable health information, but that any data sent to the Sponsor or overseas will be de-identified. If applicable, please state that coded data may be shared in the future with other qualified research groups not connected to the current study.
15. Consent: Please state explicitly that coded data will be sent overseas and may be shared with researchers not involved in the current study (if applicable).

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

1. The consent page states samples will be stored for 10 years, however the body of the PIS states 15 years. Please amend for consistency.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee.
* Please upload a confirmation letter of SCOTT approval.
* Please upload the updated insurance certificate.

After receipt of the information requested by the Committee, a final decision on the application will be made by Dr Pauline Boyles and Assoc Prof Mira Harrison-Woolrych.

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| **3** | **Ethics ref:** | **20/STH/13** |
|  | Title: | Cognitive and behavioural profiles of children in Tamaki |
|  | Principal Investigator: | Dr Alison Leversha |
|  | Sponsor: |  |
|  | Clock Start Date: | 23 January 2020 |

Alison Leversha and Alison Burge and Liz Court were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The Welcome to School (WTS) and Welcome to School Follow up Projects assessed children at schools in Tamaki. The study identified issues with low language skills, difficulty learning and achieving at school, and some children operating 18 month-two years behind expected.
2. The children are now 8 years old and in year 3 of school. Most are receiving no additional support but continue to achieve significantly below age-equivalent peers in other communities.
3. The study aims to identify the level of need in this cohort of children, and facilitate intervention and supports where possible.

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 how the children/families will be approached for this particular study, and who will make the approach. The Researcher stated that in the previous two studies the researchers went through the schools. In this study they will be directly contacting the families of children involved in the earlier study, as they have already had substantial contact with them in the past.
2. The Committee asked if there is any risk of coercion, given that the same researcher would be contacting families. The researcher acknowledged that risk and relationship, but stated that the prior relationship was important. The Committee stated that the researcher contacting the families must make it very clear to the children and their families that they are under no pressure to take part in this study.
3. The Committee asked how the participants were chosen, as only half of the cohort from the previous study is being included in this study. The researcher explained that a large proportion of the cohort dropped off either due to not providing consent or because of timing issues. The Committee expressed concern that the recruitment method could bias the study results, and suggested sending a letter to all of those participants included previously. The researcher stated that a letter was likely to yield only a minimal response from those whose children had not previously participated.
4. The Committee stated that, from the application form, it was not clear what the children are being asked to do. The Researchers explained that children will be asked to complete a Wechsler Intelligence Scale, which takes around 45 minutes, and they will also be conducting a test of the child’s attention, which is a fun task. The Committee asked why the neuro-psychology testing is considered an intervention. The Researcher explained that it is the start of an intervention. The Committee disagreed and considered the neuro-psychology testing an active assessment, which does not entail the same ethical issues as a typical intervention study.
5. The Committee noted that there are very limited disability support services available to these children, which poses an ethical issue. It asked how the researchers will ensure that the children are provided with sufficient support once issues are identified. The Committee used foetal alcohol syndrome as an example of a diagnosis for which there are limited supports/treatment available. The Committee asked whether the stigma of these issues would outweigh the benefits of the diagnosis if treatment /support services were not available.

The Researchers agreed that supports may not be available but explained that identifying and describing those needs is the first step, and that children would be referred for treatment and supports where available. The Researcher argued for the need to study these issues and identify their needs in order to make a case for improved support services. The researcher also stated that, due to the issues these children are experiencing at school, they are already stigmatised.

1. The Committee asked for further information about the Researcher’s intent to video record participants.
2. The researcher explained that the video recording is to capture a narrative. The recordings are only shared within the research group. Participants would be asked to give specific consent if the Research team wanted to use the recordings for teaching purposes.

The Committee asked about the recruitment of the teachers and whether they had the resources to participate. The Researchers stated that there is not a specific resource allocated to the teachers, but that the schools are enthusiastic to participate. The researchers further stated the importance of conducting the study in low-decile schools to capture those students who would not otherwise be receiving help. The researchers further stated that as the study is spread across 10 different schools, the number of assessments for each teacher is reasonable.

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 researcher confirmed that data would be kept for 10 years after the last participant turns 16, and that this included the video recordings. The Committee asked for the recordings to be transcribed and the videos deleted earlier, to minimise the risk of privacy breach. The Committee also asked that potentially identifying material on the recordings, such as names and addresses, be deleted from the transcript.
2. The Committee noted the response to r.2.4.1 of the application form, which states that all data will be retained in identifiable form. The researcher confirmed that the data set would retain participants’ NHI numbers The Committee stated that this was not acceptable and the study data set must be de-identified.
3. The Committee asked for identifiers, including NHI and full date of birth, to be stripped from the dataset prior to analysis and for participants to be identified by a unique participant ID. The Committee requested that this process is outlined in the protocol.
4. The Committee noted the response to r.2.3.1 of the application form, which states that no surveys or questionnaires would be undertaken during the study. The Researchers confirmed that questionnaires are intended to be used.

The Committee stated that all intended questionnaires must be reviewed and approved by HDEC prior to use, and requested that these be submitted with the response to provisional approval.

The Committee identified the following issues with the Family Information Sheet and Consent Form and requested the document be amended accordingly:

1. The PIS is very dense. Please break up the paragraphs into smaller sections and use bullet points where appropriate, to improve ease of reading.
2. Please make it clear that the child can decline to take part in the study, even if the family give consent for participation.
3. Please state clearly what the purpose of the study is for the researchers, i.e. what the study question is. This should be stated early in the document.
4. Risks/benefits section: should acknowledge that there are risks (for example, whakama) and that there may be no benefit to participants or their whanau.
5. Please make it clear that, even if an issue is identified for a participant, there may not be any treatment or support services available to access.
6. Please make it clear that the iPad will be used to record participants. Please also provide clear information about how long it will be retained for, who will have access to it, if it will be transcribed, and how confidentiality will be protected.
7. Please state that each participant’s assessment will be entered into his / her medical record and provided to the GP (and school if this is intended).
8. Please state that each participant’s identifying information will be replaced with a study code to protect confidentiality before the study data is analysed.
9. Please state that, should a participant withdraw from the study, any information already collected will continue to be analysed.
10. Please add more information to the child assent form, and explicitly that the child does not need to participate even if their parents want them to.
11. Please delete all yes / no tickboxes from the consent form unless they are truly optional.

The Committee identified the following issues with the Participant Assent Form and requested the document be amended accordingly:

1. Please state what the purpose of the study is for researchers.
2. Please make it clearer what the child will be expected to do and how long it will take.
3. Please make it very clear that the child can decline to take part, even if his/her family want them to participate.

Decision

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

* Please upload all surveys/questionnaires that will be used.
* Please update the protocol, specifying that data will be kept for 10 years after the last participant turns 16, and outlining the process for how data will be de-identified, including the transcription of videos.
* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee.

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

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| **5** | **Ethics ref:** | **20/STH/18** |
|  | Title: | Dietary sodium and potassium intakes in children |
|  | Principal Investigator: | Dr Helen Eyles |
|  | Sponsor: |  |
|  | Clock Start Date: | 30 January 2020 |

Dr Helen Eyles was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. In children, diets high in sodium and low in potassium lead to high blood pressure, which tracks into adulthood and increases the risk of heart disease. As preferences for salty foods begin early in life, children are an important group to consider. However, little is known about the sodium and potassium intakes or blood pressure of NZ children.
2. The study aims to complete a mixed-method cross-sectional survey of the sodium and potassium intakes and blood pressure of 300 school children aged 8 to 11 years via gold standard 24-hour urine collection. The main food sources of these nutrients will also be determined by 24-hour dietary recalls completed with children and their parents/caregivers. Differences in nutrient intake and sources by gender, ethnicity, household income, and by level of deprivation will be explored.
3. A Pacific sub-study is planned with interviews and focus groups with a subgroup of Pacific children, Pacific parents/caregivers and school teachers.
4. Schools will be approached through the principal or through a pre-existing relationship through the heart foundation. Principals, teachers, parents / caregivers and children can opt in or out of study participation.

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 why urinary sodium and potassium levels need to be measured, given these studies have been done overseas and it is already known which foods are high in potassium and sodium.

The researcher stated that it is not known what children are eating in New Zealand, and that diets have changed significantly since the last major surveys. Statistics such as blood pressure levels have also not been looked at in New Zealand children.

1. The Committee noted that the PISCF states that 24-hour urine collections may be completed over the weekend. The Committee stated that 24-hour urine collections could be stigmatising and difficult for children/teachers to manage if undertaken at school, and asked whether all urine collections should be completed during the weekend.

The researcher stated that most children collected urine at school in the pilot, and it did not cause any problems. The researcher acknowledged the committee’s concerns but suggested that giving the option to collect urine either way was reasonable.

1. The Committee asked who would manage collection and storage of urine samples at school.

The Researcher stated that while this is decided together with the schools, previously there would be a designated bathroom at the school, in which bottles of urine would be left. The Committee expressed concern that mistakes could happen, for example participants using incorrect bottles. The researcher acknowledged that these mistakes could happen but that the procedures in the pilot study appeared to work well.

1. The Committee asked why children with high blood pressure are being excluded from the study (as stated in the PIS).

The Researchers stated that this was not intended, and that participants with blood pressures over a protocol-specified level would be referred to the GP or school nurse.

1. The Committee asked whether individual participant results will be shared with school staff or board of trustees.

The researcher confirmed that no individual results will be shared with these groups.

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 incorrect answers had been provided to several stem questions in the application form, resulting in a number of important sections of the form not being populated. This includes the response to questions D and G. The application cannot be adequately assessed in the absence of these sections.
2. The Committee stated that the Pacific aspect of the study was not well-described or justified in the current application. The researcher stated that the PhD student named in the application would conduct a qualitative sub-study involving pacific children.

The Committee stated that a separate HDEC application may be more appropriate for the PHD project. The Researcher agreed with this approach.

1. The Committee asked how Researchers would manage children for whom abnormal results of potential clinical significance were recorded. The Researchers explained that the results would be sent back to families at the end of the study along with the WHO dietary recommendations. The Committee asked that GPs also be notified, as they are best placed to arrange appropriate follow-up and ongoing management.
2. The Committee noted that no response had been provided to question r.2.3.1., regarding the use of surveys or questionnaires in the study. The Committee stated that any surveys / questionnaires must be submitted for HDEC approval prior to use.
3. The Committee noted that the response to question r.2.5 states data will be retained for a minimum of six years. The Committee stated that data must instead be retained for at least ten years after the youngest participant turns sixteen.
4. The Committee noted that no age-appropriate child assent form(s) had been submitted for assessment and stated that these were required for the current study.

The Committee identified the following issues with the Family Information Sheet and Consent Form and requested the document be amended accordingly:

1. All PIS documents:
   * Page 2 of all PIS documents: it is stated "conduct seven focus groups across all years and ethnic groups". Elsewhere it seems that only Pacific families are involved in the focus groups. Please amend if this is not accurate.
   * Please add information in all PIS documents about the collection and storage of qualitative data, the types of questions asked, and the activity-based approach in the focus groups for children.
   * Please add a Maori contact to each PIS, and consider a Pacific contact for the Pacific focus groups.
2. Please upload a PIS specifically for children.
3. CF for BOT and Principal: please include information about the qualitative component for teachers or children.
4. PIS/CF for parent/caregiver:
   * Please add information about what parents might be asked in the interview, or what their child might do (or be asked) in the focus group. Please state clearly whether the interview is by phone or face to face.
   * Please state clearly that urine collection can happen at school or at home.
   * Please state clearly that the child can say no, and that if they do, they will not be part of the study.
   * Consent Form: "before data is analysis" should be "before data are analysed".

Decision

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

* Consent must be informed. Due to the lack of a PIS specifically for children, as well as other areas where further information was needed in the PIS documents, the Committee was not assured that this standard would be met (*National Ethics Standards* para *7.15 – 7.8).*
* All relevant questions in the application form should be completed in a manner that is reasonably likely to allow the HDEC to make a final decision on the application the first time it is considered (*Standard Operating Procedures for Health and Disability Ethics Committees* para *42.3*).

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| **6** | **Ethics ref:** | **20/STH/20** |
|  | Title: | Comparison of Tretinoin capsules in Healthy Male Subjects. |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Douglas Pharmaceuticals Ltd |
|  | Clock Start Date: | 30 January 2020 |

Dr Noelyn Hung was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This study will evaluate the relative bioavailability of a marketed tretinoin 10 mg capsule versus a new tretinoin 12 mg capsule in healthy male subjects administered under fasting conditions. Tretinoin is a known teratogen, thus only males will participate in the study.
2. The Committee commended the Researcher on a well-written application and PISCF.

Summary of outstanding ethical issues

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

1. Please separate risks of the study into ‘common’ and ‘very common’ side-effects, and add percentages if available.
2. Please change “alcohol restriction *until 12 hours*” to “until *the last P-K sample*”
3. Please proofread for typos and spelling mistakes.
4. Please explain the term pharmacokinetic when it is first used.
5. Page 2: what will my participation involve: correct or otherwise explain Day -1 to Day 2 would be greater than 24 hours

Decision

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

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

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| **7** | **Ethics ref:** | **20/STH/1** |
|  | Title: | CREATE (Community deRivEd AutomaTEd insulin delivery) trial |
|  | Principal Investigator: | Dr Martin de Bock |
|  | Sponsor: | University of Otago |
|  | Clock Start Date: | 06 February 2020 |

Dr de Bock, Renee Meier and Mercedes Burnside were present in person for discussion of this application.

Potential conflicts of interest

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

Devonie Waaka declared a potential conflict, and the Committee decided that it was non-substantial and that she would be able to participate in the discussion of the application.

Summary of Study

1. Freely available open-source algorithms which have the ability to individualise algorithm parameters paired with commercial insulin pumps and continuous glucose monitoring make up the so-called “do-it yourself” (DIY) approach to automated insulin delivery. Limited data on the DIY approach have shown promising results, but data from a large randomized control trial are lacking.
2. This study is an open-label, randomised trial in participants with type I diabetes aged 7 – 70 years. The trial will compare the Android Artificial Pancreas System algorithm paired with the DANA-I insulin pump and Dexcom G6 continuous glucose monitoring system (together named AnyDANA-Loop) to sensor augmented pump therapy. The primary outcome will be time in sensor glucose range. Long-term safety will also be assessed over a six-month follow-up phase. Secondary outcomes include psycho-social factors and platform performance. Analysis of online collective learning is planned.

Summary of resolved ethical issues

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

1. The Committee queried the amount of data available regarding the safety of the algorithm. The researchers stated that they are very confident of the algorithm’s safety as there is significant real-world experience with the algorithm. The researcher stated that the algorithm is open-source and has been used by thousands of people with type I diabetes, with de-identified glucose data uploaded to open-source databases. Although there have been no SAEs associated directly with the algorithm, there have been no formal clinical trials comparing the algorithm with other automated insulin delivery systems.
2. The Committee asked whether real-world experience with the algorithm included children in the age range proposed for the current study.

The researcher confirmed this.

1. The Committee asked whether the entire AnyDANA-Loop system was being assessed in the current study.

The Researcher explained that the algorithm is the only part being tested, as the insulin pump and continuous glucose monitor (CGM) are routinely used overseas as standard of care.

1. The Committee asked about the CGM in the study.

The Researcher explained that the CGM used in the study is the best on the market and that there is data to support that claim, which provides a benefit to participants.

1. The Committee asked whether study participation would result in high phone data usage, which may be unaffordable for some participants.

The Researchers explained that Vodafone is co-sponsoring the study and will provide participants with required data plans and mobile phones. They further stated that phone data required for study purposes is relatively minimal.

1. The Committee asked why the proposed interviews were to be conducted solely in the AnyDANA-Loop group.

The researcher explained that the control arm is an established treatment and interviewing participants receiving the control treatment would not provide any useful data. The interview component was not intended to provide any comparative analysis between the two groups.

1. The Committee noted that the response to p.4.1 stated that kaupapa Māori methods would be used in the study and asked for clarification.

The researcher stated that kaupapa Māori methods would not be used.

1. The Committee asked if participants would be reimbursed.

The researchers explained that participants will be given $20 per visit to cover transportation and parking costs.

1. The Researchers stated that email addresses were required when setting up the food diary app required for the study. The Committee agreed that was a potential privacy issue.

The Researcher stated that study-specific addresses would be created for this purpose.

1. The Committee questioned the lack of pictures/diagrams included in the Younger Child PIS. The Researchers explained that the PIS is intended for parents to go through with the children.

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 the justification for conducting the study in children, rather than in adults. The Researchers explained that this is a predominantly paediatric disease, and conducting the study in adults would delay the collection of data relevant to the paediatric population, potentially delaying more effective treatment for children. Furthermore, there is pre-existing real-world safety and efficacy data for this algorithm with children.   
   The Committee asked that older children be enrolled before younger children. The Committee stated that more detailed information was required regarding the collection and analysis of information for the qualitative study.
2. The Researchers asked whether technical information about the AnyDANA-Loop system should be included in the protocol, as they stated that the system is likely to be amended during the study. The Committee stated that this information can instead be included in a study manual. Future changes to the manual would not require submission to HDEC unless criteria for a substantial amendment were met.
3. The Committee noted that the User Guides were written in complex and often technical language that may be overwhelming for participants / caregivers. The Committee asked that the User Guides be simplified and lay language used where possible, to improve readability.
4. The Committee asked that the initial approach regarding study participation be made by a member of the patient’s clinical care team.
5. The Committee noted that questionnaires would include depression scales, and asked how quickly these would be looked at. The Researcher stated that the questionnaires will be reviewed and flagged within a fortnight, and that those participants would be contacted and referred to the GP or specialist mental health services, as appropriate.   
   The Committee asked for this to be detailed in the protocol and PISCF documents.

The Committee identified the following issues with the Participant Information Sheet and Consent Forms and requested the documents be amended accordingly:

1. Please re-title as “CREATE interview” or “CREATE experiment” for ease of reference.
2. The diagram on page 3 appears to be cut and pasted from the protocol and is not appropriate for use in a lay document. Please amend.
3. The diagram on page 4 appears to show that wifi is required to interact with the phone in order to modify insulin delivery. Please amend to show that the system also works with Bluetooth.
4. Please ensure a risks/benefits section is included in all PISCFs. The principal risk is unexpected hypoglycaemia or hyperglycemia, which is currently not included in all documents.
5. Please state that, if study assessments reveal a concern about the participant’s mental health, the participant’s GP or mental health services will be contacted.
6. Please provide clearer information is required about privacy and confidentiality. This should include: who has access to identifiable information (including for audit); how and when data is de-identified; where data is stored (clouds etc); who potentially has access to it (device manufacturer, regulatory agencies, other researchers....); privacy provisions for the apps used; and the rights of access to and withdrawal of personal data.
7. Please state that data needs to be retained for 10 years after the youngest participant turns 16.
8. Please state whether (and how) interviews will be recorded and how long the recording will be retained for. If audio or digital recordings are intended, please state whether these will be transcribed. Please also confirm that any identifying information in the recordings (such as references to names or addresses) will be deleted from the transcript.
9. Please delete the sentence ‘If you think you have been hurt’ from the Younger Child’s interview assent form.
10. Please add an “if you need an interpreter” statement to the Interview consent form.

Decision

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

1. Please update the protocol, ensuring that
   * Older children are enrolled before younger children.
   * The initial approach to potential participants is made by a member of the patient’s clinical care team.
   * A plan for contacting/referring those who indicate depression is outlined.

* Please update the user manual for the AID algorithm.
* Please create a user manual for the AnyDANA-Loop system
* Please amend the information sheet and consent forms for both the main study and interview, taking into account the suggestions made by the Committee.

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

## 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:** | 10 March |
| **Meeting venue:** | Sudima Hotel, Christchurch Airport, 550 Memorial Drive, Christchurch |

1. **Problem with Last Minutes**

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

The meeting closed at 2:45pm.