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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 20 July 2021 |
| **Meeting venue:** | <https://mohnz.zoom.us/j/7894526927> Zoom Meeting ID: 789 452 6927 |

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| **Time** | **Item of business** |
| 1.00pm | Welcome |
|  | Confirmation of minutes of meeting of 15 June 2021 |
| 1.20pm | New applications |
| 1.20-1.45pm1.45-2.10pm2.10-2.35pm2.35-3.00pm3.00-3.20pm3.20-3.45pm3.45-4.10pm4.10-4.35pm4.35-5.00pm5.00-5.20pm5.20-5.45pm5.45-6.10pm6.10pm | 21/NTA/105 21/NTA/107 21/NTA/113 21/NTA/109 Break (20 minutes)21/NTA/110 21/NTA/111 21/NTA/112 21/NTA/108 Break (20 minutes)21/NTA/114 Discussion of study complaintMeeting ends |

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| **Member Name**   | **Member Category**   | **Appointed**   | **Term Expires**   | **Apologies?**   |   |
| Dr Karen Bartholomew  | Non-lay (intervention studies)  | 18/07/2016  | 18/07/2019  | Present  |   |
| Mrs Kate O'Connor  | Lay (consumer/community perspectives)  | 29/01/2020  | 29/01/2021  | Present  |   |
| Dr Kate Parker  | Non-lay (observational studies)  | 11/02/2020  | 11/02/2023  | Present  |   |
| Ms Rochelle Style  | Lay (ethical/moral reasoning)  | 14/06/2017  | 14/06/2020  | Present  |   |
| Ms Catherine Garvey  | Lay (the law)  | 19/03/2019  | 19/03/2022  | Present  |   |
| Dr Sotera Catapang  | Non-lay (observational studies)  | 11/02/2020  | 11/02/2023  | Present  |   |
| Dr Michael Meyer  | Non-lay (health/disability service provision)  | 11/02/2020  | 11/02/2023  | Present  |   |

## Welcome

The Chair opened the meeting at 1pm 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 15 June 2021 were confirmed.

## New applications

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|  **1**   | **Ethics ref:**   | **21/NTA/105**  |   |
|   | Title:  | Pan tumor Nivolumab Rollover Study  |   |
|   | Principal Investigator:  | Dr Richard North  |   |
|   | Sponsor:  | Bristol-Myers Squibb  |   |
|   | Clock Start Date:  | 08 July 2021  |   |

Dr Richard North 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 Study

1. This study is a long-term follow-up of cancer survivors who have participated in trials Investigating Nivolumab. There is a trend emerging favouring continuous Nivolumab and this open label roll-over study is to establish long-term safety and optimal treatment duration. There will be 1231 participants of which 20 are in New Zealand.

Summary of resolved ethical issues

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

1. The researcher confirmed that participants, after completing a parent trial, will continue to receive Nivolumab during this follow up study.
2. The researcher clarified the study purpose, advising that it is predominately to understand survival and safety outcomes through a ‘catch-all’ long term follow up of participants who have completed parent trials involving Nivolumab. He added that it is also an opportunity for participants to continue (trial-funded) Nivolumab treatment after their (two-year) parent trial finishes.
3. The Committee advised that it was unclear in the protocol what safety elements are being measured, besides survival (e.g. unexpected events) because no imaging is planned. The researcher confirmed that they will be undertaking an adverse event review during the course of the follow-ups to capture any post (two year) trial/treatment events that may have occurred.
4. The Committee queried if there are any safety signals the research team is concerned about in the post two-year period. The researcher advised that they are not anticipating any safety issues.
5. The Committee were concerned that the study presents as (post marketing) phase four but is recorded as phase two which presents safety and ethical concerns depending on the phase (e.g. MNZ guidelines do not apply to phase four). The researcher stated that the umbrella for studies collected up a range of phase two to three studies as follow on and therefore they had included phase two as the minimum. After discussion, the Committee was satisfied that the relevant safety issues, with regards to a phase two and phase three protocol, have been sufficiently addressed by the researcher, and that ACC-equivalent compensation for treatment injury would be provided.
6. The Committee noted the lack of transparency of the eligibility criteria the sponsor is using to select parent studies for inclusion in this follow up study. Concerns were discussed about the potential for biasing study results with sponsors picking and choosing studies, however, without condoning it, the Committee acknowledged that this is typical practice in open label extension studies and the research team has no influence on the selection criteria or process, although the Sponsor does.
7. The Committee noted that so far there is only one (concluded) parent study in New Zealand that is eligible to roll over into this study and advised that HDECs will need to be notified through the post approval (amendment) pathway should any other New Zealand trials become eligible in the future.
8. The Committee noted that the descriptions around privacy policies for Greenphire in the Participant Information Sheet and Consent Form (PIS/CF) may not be consistent with the policies on Greenphire’s website. The researcher clarified that their site does not use Greenphire and therefore it will not be relevant for the New Zealand arm of the study.

Summary of outstanding ethical issues

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

1. The researcher confirmed that the proposed 20 candidates for the follow-up study are known to the research team as they are coming from other Nivolumab trials. The Committee was concerned that the material submitted with the study was overly marketing intensive given that advertising is not required for the purposes of recruitment. The Committee stated that the newsletters and supplementary material submitted, therefore, will not be approved as they are not relevant to the New Zealand study context.
2. The Committee requested clarity on what the BMS Study Connect description is and what it will be used for.
3. The Committee advised that the study documentation needs to be customised to reflect the New Zealand context and recommended a protocol addendum addressing this, detailing how the recruitment and follow up processes will work in New Zealand given there is only one New Zealand study eligible for the roll-over study.
4. The Committee stated that the data and tissue management details in the protocol are insufficient for the New Zealand context. Please supply a Data and Tissue Management Plan appropriate to the New Zealand arm of the study that complies with *National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 12.15 and 14.17.* For guidance, please see the [Data and Tissue Management Plan template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/hdec-data-tissue-management-template-oct2020.docx) available on the HDECs website.
5. The Committee advised that all researchers conducting health research in New Zealand must collect good-quality ethnicity data. *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 9.20).* Please ensure ethnicity data is collected at the local (New Zealand) sites.
6. The Committee stated that if the research team intends to use samples from an optional biomarker for future unspecified research a separate PIS/CF is required that complies with *National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 7.58*. For guidance, please see the [Future Unspecified Use of Tissue PIS/CF template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/future-unspecified-use-tissue-piscf-template.doc) available on the HDECs website.

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

1. Please customise the participant facing documentation for the New Zealand audience.
2. Please add the sponsor’s address on page 1.
3. Please add information about what pre-trial participant data will be accessed and include a consent form clause for this.
4. Please identify which countries the data will be sent to (e.g. India and the United States).
5. Please amend the statement referencing withdrawal being made in writing as it can be provided verbally in New Zealand (page 2).
6. Please proofread participant facing documents and correct typos.
7. Please state the approval situation for Nivolumab in New Zealand under the ‘Purpose’ section on page 2.
8. Please explain, in the body of the participant information sheet, the possibility that participants’ general practitioners will be informed of abnormal test results.
9. Please explain that participants may request access to the results of their screening and safety tests during the study and any implications of this that they should be made aware of.
10. Please remove reference to abstinence being an acceptable form of contraception as this is not recognised by HDECs as reliable.

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 2019, 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 2019, para 9.7).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Dr Karen Bartholomew and Mrs Kate O’Connor.

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|  **2**   | **Ethics ref:**   | **21/NTA/107**  |   |
|   | Title:  | SPLIT ENZ  |   |
|   | Principal Investigator:  | Mrs Lynsey Sutton  |   |
|   | Sponsor:  | University of Otago  |   |
|   | Clock Start Date:  | 08 July 2021  |   |

Lynsey Sutton and Paul Skirrow 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 Study

1. A study to evaluate the recovery of patients who have been critically ill in the intensive care unit. Involves the cognition, mental health, and physical function as well as quality of life, ability to return to work, and social aspects (Post intensive care syndrome, PICS).

Summary of resolved ethical issues

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

1. The researchers confirmed that the pilot study is part of the study and involves providing questionnaires to the first 10 study participants. The researchers added that if the pilot results show that the questionnaires are too lengthy for participants in recovery, they will reduce the number of questions and potentially discard two of the questionnaires. The researchers should submit any amendments to the questionnaires for HDEC approval.
2. The researchers confirmed that they expect to interview up to 20 participants.
3. The Committee queried if the difference in the three interview methods (e.g. face-to-face, Zoom, telephone) could influence the results of the interviews. The researchers acknowledged this and confirmed that the preferred choice is face-to-face interviews with Zoom and telephone interviews only used as back up methods in the event that in person meetings are not possible (e.g. due to Covid-19 restrictions).
4. The Committee queried who will administer the Montreal cognitive assessment questionnaire. The researchers advised that they are using a MoCA blind tool designed for telephone interviews. Paul Skirrow is a clinical psychologist trained in MoCA and will supervise the CI, Lynsey Sutton, to administer the questionnaire once she completes the pre-requisite MoCA training.

Summary of outstanding ethical issues

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

1. The Committee advised that enrolling patients in ICU prior to them being well-enough to consent for themselves requires a stronger justification than convenience for the researchers and is not a scenario that would be approved by HDECs *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, Chapter 7, particularly paras 7.4 – 7.5).* As the bulk of data collection is only required post discharge, the Committee sees no real barrier to obtaining informed consent from participants and as a result, recommends the following changes:
	* please restructure the study design so that patients can consent for themselves once they have recovered sufficiently to do so
	* please undertake a retrospective review of participants’ medical records upon consent being obtained
	* please ensure this structural change is reflected in the protocol and the participant-facing documentation.
2. The researchers advised that it can be difficult to reach patients after they have been transferred out of Wellington and plan to address this by following up with these patients by phone and mailing/emailing the PIS/CF to those interested in participating. The Committee was comfortable with this approach and requested that this recruitment strategy is further refined and detailed in the protocol.
3. The Committee noted that the Qualitative Interview Participant Information Sheet and Consent Form (PIS/CF) suggests that whānau/family members will be invited to attend the interview and have questions asked about their experience. The Committee advised that as gathering data about the whānau/family member makes them a participant in the study, they require their own PIS/CF detailing how their information is being collected and used, etc.
4. The Committee queried if the researchers plan to address the peer reviewer’s comment on the feasibility of reaching the proposed sample size within the six-month recruitment period given the high mortality rate of critically ill patients. The researchers advised that they recognise the need to over sample due to the high mortality rate and expect to extend the recruitment period to achieve their analysis goals. The researchers confirmed that they will make this clearer in the protocol.
5. The Committee recommended adjusting the safety escalation plan (on page 39) to remove mention of asking the whānau/family member/friend/relative about the participant’s mental health symptoms as researchers cannot talk to a participant’s whānau/family without their prior consent.
6. The Committee queried how the researchers plan to select participants for interviews that will not lead to a biased result. The researchers advised that they would not be picking and choosing the interview candidates but instead plan to interview participants as they come through for their six-month follow up, until saturation point is reached. The Committee requested that the recruitment process for the qualitative interviews is documented in detail in the protocol.

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

1. Please rework all PIS/CFs to reflect changes to the consent process (i.e. enrolment begins once the participant is well enough to consent for themselves).
2. Please remove the relative PIS/CF as this is no longer needed for consenting on behalf of the participant – or, if whānau/family will be interviewed, repurpose it to reflect the whānau/family involvement in the study.
3. Please be more explicit on what information will be collected about the participant from their medical records (e.g. outline the big categories of information), how this is done, when and who has access to it, etc.
4. Please add the following statement to the ‘Rights to access information’ sections of the PIS/CFs, ‘You also have the right to request that any information you disagree with is corrected.’
5. Please amend references to data being sent overseas as this is not applicable to this study.
6. Please remove the two bullet points under the ‘Identifiable Information’ section of the PIS/CFs as these are not applicable to this study (i.e. general practitioner and threat to public health).

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 Ms Catherine Garvey and Dr Sotera Catapang.

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|  **3**   | **Ethics ref:**   | **21/NTA/113** |   |
|   | Title:  | The Healthy New Zealand Foods Pilot Study |   |
|   | Principal Investigator:  | Dr Jeremy Krebs  |   |
|   | Sponsor:  |  |   |
|   | Clock Start Date:  | 08 July 2021  |   |

Dr Jeremy Krebs 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 Study

1. The High Value Nutrition (HVN) National Science Challenge works with scientists and businesses to add nutritional value to fresh and processed food products for the benefit of consumers whether in New Zealand or elsewhere in the world. Funded by HVN, the investigators are leading the development and implementation of He Rourou Whai Painga, an ambitious long-term multi-centre dietary intervention study that will explore whether consumption of high quality New Zealand food and beverage (F&B) products in an adapted Mediterranean-style dietary pattern improves metabolic, cardiovascular, and wellbeing profiles in people at risk of cardiometabolic disease. The current proposal describes a pilot study that will be used to finalise the study design, power calculations, and final methodology of the main intervention study, He Rourou Whai Painga.

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 the majority of issues outlined in the decline decision letter have been addressed in this resubmission with some minor issues remaining.
2. The Committee noted that My Food Bag is contracted to provide food that fits the dietary intervention being studied and participants will access the My Food Bag online ordering system to order weekly meals and snacks from a study-specific selection.
3. The Committee advised that the household members need sufficient time to consider their involvement and queried at what point they will be informed about the study and consented/assented prior to undertaking the assessments. The researcher advised that the study will be discussed with the primary adult (index) participant separately first where they will be given the relevant study material to take home and discuss with the household members. The researcher added that the household will be given the option to either return and discuss any questions they have prior to the assessments taking place or to discuss when they return for the assessment session.

Summary of outstanding ethical issues

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

1. The Committee advised that some of the language used in the five to 10-year-old assent form is too advanced for young children (e.g. physical activity, if you identify as Māori, research team etc.) and requested this is revised and simplified so that a younger person can understand it.
2. The Committee advised that the 11 to 13-year-old assent form, similarly, is too complex for this age group and requested that the language is simplified.
3. The Committee advised that the term ‘cholesterol’ may be unknown to 14 to 15-year-olds and suggested this is described more simply in this assent form (e.g. ‘a test to measure the fat content of your blood’.)
4. The Committee advised that it is not clear in the assent forms that the study is about food and not just measurement outcomes. Please amend these forms to make it clear that the study is about the family doing something different with food and that is why the child is being measured. For example, the five to 10-year-old assent form could say ‘we are doing a study about different foods that your family is going to help us with’ and include some appropriate images of Mediterranean food.
5. The Committee noted that the Main PIS/CF for the primary adult (index) participant includes a section for consenting the children, however, the adult may not be the child’s legal guardian. Please consider this scenario and update the participant information sheet and consent form (PIS/CF) accordingly to address this (e.g. provide a Parent/Guardian PIS/CF).
6. The Committee advised that all competent children/young people must provide their own informed consent and that there is no bright-line age for children consenting for themselves (e.g.16-years-old). Please consider how you will determine each individual child’s competency and subsequent consent or assent process. For guidance, please see the *National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 6.22 – 6.30).*
7. The Committee requested that the recruitment process for identifying and approaching potential participants is outlined in the protocol (e.g. enrolling participants through the CEDOR clinic and/or advertising, screening of medical records to identify eligible candidates, phoning potential participants before sending a letter of invitation).
8. The Committee requested that the Data Management Plan clearly details My Food Bag’s access to participants’ data (i.e. what data My Food Bag will have access to and how it will be used including the Survey Monkey questionnaire) and how their data will be protected. For example, providing confirmation the names and addresses will not be retained or used for My Food Bag marketing purposes and not shared in any way other than what participants have given permission for. Please also ensure that participants are made aware of what data My Food Bag will have and how it will be used etc. in the PIS/CFs.
9. The researcher confirmed that biomarkers will not be done in this study and the reference to keeping blood samples to do further testing is for study specific testing only, should they need to establish other markers. The Committee recommended the following:
	* please rephrase the blood sample/test statements on page 3 of the Main PIS/CF to make it clearer that the other tests they may happen will be directly related to this study
	* please list the other potential tests in the protocol (e.g. insulin, etc.)
	* please address this and the use of tissue generally in the Data Management Plan. For guidance, please see the [Data and Tissue Management Plan template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/hdec-data-tissue-management-template-oct2020.docx) on the HDECs website. (*National Ethical Standards for Health and Disability Research and Quality Improvement, para 14.17).*

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

1. Please update the benefits and risks section to include the risk of participants feeling they have failed if they do not stick to the diet and reference the privacy breach risk that is discussed later on in the data section.
2. Please correct the advocacy email address in the headline for the optional consent form.
3. Please either develop a separate PIS/CF or add a section to the Main PIS/CF, that details what the other adult household members participation in the study involves as it is different to the primary (index) adult and children.
4. Please include in the Main and Household PIS/CFs more information about the diary and the questionnaires including how long they will take to complete.
5. Please include the following statement under the ‘Rights to access your information’ sub section, ‘Please ask if you would like to access the results of your screening and safety tests during the study’.
6. Please include an option to the consent forms for participants to receive the results of their blood tests.

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 Michael Meyer and Ms Catherine Garvey.

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|  **4**   | **Ethics ref:**   | **21/NTA/109**  |   |
|   | Title:  | The STEP Study: Smartwatch Takiwātanga Exercise Project  |   |
|   | Principal Investigator:  | Dr Gloria Dainty  |   |
|   | Sponsor:  |   |   |
|   | Clock Start Date:  | 08 July 2021  |   |

Fatemeh Sajjadi and Liv Bruce 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 Study

1. The proposed study pilots a smart watch intervention, with the aim to promote exercise and sleep in children with Autism Spectrum Disorder/Takiwātanga. The study has three phases: pre-intervention baseline measurements, intervention, and post-intervention follow up measurements. The intervention phase involves four weeks of consistently wearing the smart watch, with four daily challenges for the child, per week. These challenges will be step count and active minute goals, to promote increased exercise in the child. Overall, the intervention is hypothesised to improve sleep and promote exercise in the participants.

Summary of resolved ethical issues

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

1. The Committee asked for clarity on how the daily tasks are customised to the individual (e.g. age or baseline activity as the peer reviewer suggests). The Researcher confirmed that they recognise that each child’s activity will be variable and that an individualised approach will be best for the participants and for measuring improvement.
2. The Committee queried the research team’s recruitment plan and how they will manage to recruit the proposed number of participants within the study timeframe. The researchers confirmed participants will be recruited via two pathways; through social media advertising and through the clinic at Dunedin Hospital. The researchers stated that they are confident they will hit their recruitment target for the following reasons:
	* the CI is a paediatrician and can identify eligible patients from her clinic
	* the research team has access to 15 eligible contacts from a previous qualitative study
	* the study population has been broadened and will include children with ADHD.
3. The Committee queried how the CI’s dual role conflict will be managed. The researchers advised that the CI will pass on potential participant contact information to the research team who will undertake all of the communication with the participant and their parents.
4. The Committee advised that any advertising material must be presented to HDECs for review. If the researchers intend to advertise, please upload the ads via the post-approval (amendment) pathway.

Summary of outstanding ethical issues

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

1. The Committee noted the researchers’ justification for choosing a broad age range (five to 12-year-olds) of participants is to determine what ages a Smartwatch is suitable for. The Committee requested clarity on why the age has been commenced at 5 years and cut off at 12 years.
2. The Committee noted that the participants will be asked to return the watch at the end of the study and were concerned with the unfairness of giving children something they may like and get attached to and then taking it away. (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 8.3).* Please revisit this decision and provide a response to the HDECs.
3. The Committee were concerned about the accuracy of Fitbit’s sleep and activity data for research purposes, especially given the involuntary movements that some autistic children have (e.g. hand flapping). The Committee stated that there are more up to data studies published on the reliability of Fitbit in a research setting than those referenced in the protocol and invited the researcher to investigate this and update the HDECs on Fitbit’s validity regarding these two points.
4. The Committee require a Data Management Plan for the lifecycle of the study to ensure the safety and integrity of participant data (including the demographic survey data). This may either be incorporated into the protocol or a separate plan, but it must be study-specific and comply with *National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 12.15a.* For guidance, please see the [Data Management Plan template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/data-only-management-template-oct2020.docx) available on the HDECs website. Please ensure the template is modified to appropriately reflect the data management requirements of this study.
5. The Committee advised that the participant information sheet and consent forms (PIS/CFs) are too advanced for even a 12-year-old and are not appropriate for children with autism who may experience literacy difficulties. Please review these and simplify the language used.
6. The Committee advised that parents/guardians require an opportunity to read the full information sheet before signing the consent form and requested the consent is transferred from the demographic survey to the PIS/CF. (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 7.15 – 7.18a).*
7. The Committee requested that the researchers ensure the task messages are fit for the audience and are submitted to the HDECs for review.
8. The Committee were concerned with the proposed prize incentive method for the following reasons:
	* it may cause the children frustration if they have not met their goal
	* parents may choose to keep their child happy and award the prize even if the goal was not met.
9. The Committee was concerned about the exercises that are being promoted (e.g. swimming, biking, trampolining) for the following reasons:
	* most of the exercises are outside activities and the cold Dunedin winter weather may dissuade participants from taking part
	* they raise an issue of equity as not every child has access to bicycles and trampolines or the swimming pool fee. (*National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 10.39).*
10. The Committee advised that the researchers should keep research data on child participants for at least 10 years after the child has reached the age of 16 years. (*National Ethical Standards for Health and Disability Research and Quality Improvement, para 6.28).*
11. The Committee advised the PIs/CIs medical indemnity certificate was not submitted and requested that this is uploaded on the portal. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 17.6).*
12. The Committee queried if the formal Māori consultation has been undertaken to ensure the study is appropriate for a New Zealand context. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 3.7).*
13. The Committee recommended that the researchers review the supported decision-making NEAC Standards for awareness and guidance for ethical management of vulnerable participants within this study. *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, chapter 6).*
14. The Committee requested that consultation with relevant autism groups is undertaken. *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, chapter 5, particularly para 5.4).*
15. The Committee advised that extending the population to include ADHD is a substantial change to the protocol. The Committee requested a justification for including this type of vulnerable population. *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 6.19).*

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

1. Please adapt the HDEC approved [PIS/CF Template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc) to your study to ensure that your information sheets comply with *National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 7.15 – 7.17.* For example, including the Accident Compensation Corporation statement and more information on participant rights.
2. Please amend the terms ‘anonymity’ and ‘anonymous’ as data collected with identifiers, cannot be described this away. Please ensure the forms in which data is collected, analysed, and stored in this study are described accurately.
3. Please make it clear which part of the study is being undertaken as part of a qualification.
4. Please amend the length of time data will be stored for from 5 years to 10 after a child has turned 16-years-old.

Decision

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

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|  **5**   | **Ethics ref:**   | **21/NTA/110**  |   |
|   | Title:  | R3R01 single dose study in healthy adults  |   |
|   | Principal Investigator:  | Dr Chris Wynne  |   |
|   | Sponsor:  | River 3 Renal Corp  |   |
|   | Clock Start Date:  | 15 July 2021  |   |

Dr Chris Wynne and Sharmin Bala 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 Study

1. The study will review the safety, tolerability, and pharmacokinetic (PK) of three different single, oral doses of R3R01 (new polymorph) across three cohorts. It is envisaged that 24 (12 men and 12 women) participants will be recruited to this study in New Zealand.

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 the researcher to explain the polymorphs and whether it is a first in human trial or not. The researcher confirmed that the polymorph is a well characterised molecule and it is not a first in human trial. Rather, the study is a low risk bioequivalence study to determine any differences in the PK properties of the two polymorph molecules after the sponsor made a change to how it is manufactured.
2. The Committee asked if there is any other relevant information available about the clinical effects of Polymorph A that would be helpful. The researcher stated that all relevant findings are included in the Investigator’s Brochure and briefly summarised in the introduction section of the protocol.
3. The Committee queried the $5m insurance cover and referenced NZACRES guidelines that suggest $10m is a more acceptable level of cover for later stage trials. The researcher responded that he considers $5m to be an adequate level of cover for this study for the following reasons;
	* This is regarded as a low risk study that is not first in human and has a low number of participants (whereas the NZACRES suggested total sum may apply to later phase studies that will have a larger number of participants).
	* The sponsor is liable for any costs over and above the $5m insurance cover.
	* The research site has an indemnity policy and would be responsible for covering costs should the sponsor not honour its obligations.
4. The Committee was comfortable with the researcher’s response that $5m is an adequate level of insurance for this particular study and noted that the researcher will advise sponsors to increase their indemnity cover for future studies.

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 there are no safety concerns for this drug and that participants are required to stay for two nights to ensure that the PK samples are taken correctly, rather than for safety reasons. The Committee requested that this is explained to participants in the participant information sheet and consent form (PIS/CF).
2. The Committee requested that the researcher refrains from using the word ‘ensure’ with regards to the statement that ‘data sovereignty principles are in place to ensure the data generated is protected and may benefit Māori’ as this cannot be guaranteed. The researcher advised that he will update their master template to reflect this change for the current study and future studies.
3. The Committee queried the reference to data being sent to Australia only in section 8.3 of the data and tissue management plan (DTMP). The researcher confirmed this was an error and will correct it.
4. The Committee noted that the DTMP mentions future unspecified research (FUR) but the PIS/CF does not and requested that this inconsistency is reconciled in the study documentation.
5. The Committee advised that the samples include too many identifiers (e.g. study number, year of birth, initials, and gender) and requested that these are reduced to as few as possible. *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 12.11-12.14).* Please update the DTMP and PIS/CFs accordingly.

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

1. Please remove information that is not specifically helpful to participants to ensure they are not overburdened with irrelevant information (e.g. remove reference to ACC IR330C).
2. Please include Hepatitis B and C as notifiable diseases in addition to HIV.
3. Please clarify that the studies undertaken in volunteers is only for polymorph A so that participants do not think that the polymorph they will be receiving has been studied.
4. Please make it clear that the approved Covid-19 vaccine in New Zealand is an mRNA vaccine so participants know what restrictions apply (page 8).
5. Please amend section 7.2 because a therapeutic study cannot be stopped for reasons of commercial interest in New Zealand. *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 11.37).*
6. The Consent Form mentions collecting health information. Please include where this information will be collected from in the body of the information sheet (e.g. general practitioner, etc.)
7. Please remove reference to abstinence being an acceptable form of contraception as this is not recognised by HDECs as reliable.
8. Please add the word ‘data’ to the following section heading on page 10, ‘What could happen to me by giving these biological samples?’
9. Please include the names of the labs and countries where the samples are being sent to (page 10).
10. Please include the following statement under the ‘Rights to access your information’ sub section, ‘Please ask if you would like to access the results of your screening and safety tests during the study.

Decision

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

* please address all outstanding ethical issues, providing the information requested by the Committee.
* please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, paras 7.15 – 7.17).*

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|  **6**   | **Ethics ref:**   | **21/NTA/111**  |   |
|   | Title:  | (duplicate) Phase III Study assessing the efficacy, safety and immunogenicity of SOK583A1 versus Eylea® in patients with neovascular age-related macular degeneration  |   |
|   | Principal Investigator:  | Dr David Worsley  |   |
|   | Sponsor:  | Syneos Health New Zealand Limited  |   |
|   | Clock Start Date:  | 08 July 2021  |   |

Dr David Worsley and Reenu Arora 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 Study

1. The study is a 52-week randomised double masked two arm parallel study comparing study drug efficacy, safety and immunogenicity of SOK583A1 with Eylea® - an approved treatment - in 460 patients over 50-years-old with neovascular age related macular degeneration.
2. This is the first in human study of SOK583A1. The extensive available data demonstrate structural and functional (in vitro) similarity between SOK583A1 and Eylea®. Patients will be randomised to either drug on a 1:1 ratio and will receive a single intravitreal injection at baseline, week 4, 8, 16, 24, 32, 40 and 48 weeks.
3. Participants will have efficacy and safety assessments prior to study treatment, including visual acuity test, blood and urine tests, physical examination, medical history and vital signs, complete ophthalmic exam, measures, and photographs. Both drugs will be given by unmasked investigators. All other study procedures will be conducted by masked investigators who will not know which treatment the participant is receiving.

Summary of resolved ethical issues

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

1. The Committee noted that this was a resubmission of an application that had been considered and declined by the Northern B HDEC. The Committee thanked the researchers for making the changes requested by the Northern B HDEC.
2. The Committee asked if the researchers will exclude participants on blood thinning medication. The researchers stated that they will not exclude these participants because blood thinners are not considered to carry extra risks for the intravitreal injection.
3. The Committee asked if participants can receive Eylea® on the non-study (placebo) eye if it also develops macular degeneration. The researchers confirmed that this is possible because the study is being funded by the sponsor. It would not be possible outside of the study as the treatment is not currently funded in New Zealand.

Summary of outstanding ethical issues

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

1. The Committee requested that the researchers refer to the current *National Ethical Standards for Health and Disability Research and Quality Improvement 2019* throughout the documentation. Currently, there is incorrect reference to the ‘Ethical Guidelines for Intervention Studies, National Ethics Advisory Committee (2012, updated 2019)’.
2. The Committee asked the researchers to tailor the Participant Information Sheets and Consent Forms for the optional sub-studies precisely to each sub-study. It is not sufficient to copy and paste the data privacy sections from the main Participant Information Sheet and Consent Form as they are not relevant to each optional sub-study and do not cover everything specifically.
3. Please ensure that all Participant Information Sheets and Consent Forms comply with the Health Information Privacy Code 2020 and Privacy Act 2020. Please note that there is a new right under the Privacy Act 2020 about data being sent overseas and there are warning statements that must be included for this. Refer also to the [*National Ethical Standards for Health and Disability Research and Quality Improvement 2019*](https://neac.health.govt.nz/national-ethical-standards/part-two/12-health-data/).
4. The Committee referred to the optional tissue and data for future unspecific research Participant Information Sheet and Consent Form. Please refer to paragraphs 7.57 and 7.58 of the NEAC Standards as linked in the point above for guidance on what is required specifically and ensure the document complies with these.
5. The Committee referred to the optional pharmacokinetic (PK) sub-study. The Committee stated it would be helpful to clarify and differentiate between what is happening in the main study and in this sub-study. For example, on page 5 of the Participant Information Sheet for the PK sub-study, it states that risks are possible side effects of tests done during the sub-study. However, the researchers confirmed that only blood tests will be conducted. Please state the risks associated with blood tests instead.
6. The Committee referred to the Data and Tissue Management Plan (DTMP). The Committee noted that the researchers stated that organisational data governance oversight was not applicable. However, the Committee would like assurance that there is relevant data governance oversight since there will be three separate private clinics for the study. There needs to be data governance policies and processes in place at each site.
7. Please ensure that the DTMP is consistent with the Participant Information Sheet and that it is also internally consistent. For example, the DTMP states that data will be added to larger datasets, however, this is not stated in the Participant Information Sheet. The DTMP also states on page 9 that de-identified data is stored long-term by the Sponsor in secure, cloud-based and sponsor company server storage indefinitely and yet elsewhere, the DTMP states that de-identified data will be retained for 15 years. These inconsistencies must be rectified, and the Participant Information Sheet should reflect all relevant information from the DTMP.
8. The Committee referred to the Patient Brochure. This document appeared to be a short form version of the main Participant Information Sheet. The Committee advised it would not approve a short form version as the main Participant Information Sheet should be sufficiently understandable. The Committee noted that the Patient Flowchart document and Participant Individual Study Results template were acceptable.
9. The Committee noted that several different logos are used in the documentation and that this may cause confusion for participants. The Committee asked who the New Zealand sponsor is. The researchers stated that Syneos Health New Zealand Limited is the New Zealand sponsor. Hexel AG and Sandoz Incorporated are the international sponsors. The Committee queried how important it is for participants to know about the different companies’ involvement at various levels of the study. This becomes relevant in regards to how much data the researchers are/are not sharing with the other companies. Please include this information in the DTMP and Participant Information Sheet.
10. The Committee noted that for insurance/compensation, the researchers have referred to Medicines New Zealand Guidelines. However, these guidelines exclude compensation for comparators. Please provide evidence that any treatment injury occurring during the study will be covered by insurance.
11. The Committee asked what the researchers will do if participants develop serious side effects such as cataract formation, bleeding from the eyes, and retinal detachment etc. The researchers stated that if there are any complications the participant will be withdrawn from the study. The researchers also noted that the risk of a significant complication from an injection into the eye is very low. Please include this information in the study documents.
12. The Committee noted that independent peer review has not been provided. Please refer to the [HDECs guidance and template](https://ethics.health.govt.nz/guides-templates-and-forms/scientific-peer-review-submissions-guidance/) and provide a copy when available.

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

1. On pages 11, please rename the title of the table to reference the compound which is in both SOK583A1 and Eylea®. There cannot be known side effects of the study drug yet because it has not been studied before. Only the risks of Eylea® are currently known.
2. Please amend the Consent Form to state that blood and urine samples will be taken locally but results will be sent overseas.

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 all the participant information sheets and consent form, especially the sub-study Participant Information Sheets and Consent Forms, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement 2019, para 7.15 – 7.17).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Dr Sotera Catapang and Ms Rochelle Style.

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|  **7**   | **Ethics ref:**   | **21/NTA/112**  |   |
|   | Title:  | (duplicate) GDM and school age outcomes (GiST)  |   |
|   | Principal Investigator:  | Dr Jane Alsweiler  |   |
|   | Sponsor:  | University of Auckland  |   |
|   | Clock Start Date:  | 08 July 2021  |   |

Dr Jane Alsweiler 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.

Dr Michael Meyer declared a potential conflict of interest and the Committee decided he should not contribute to the discussion.

Summary of Study

1. This is a matched cohort study (GiST) comparing gestational diabetes mellitus (GDM)-exposed with non-GDM-exposed children to determine the long-term effects of gestational diabetes on school age outcomes (neurocognitive function, health and wellbeing, cardiometabolic function). This ethics application related specifically to the recruitment of the matched control group.

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 participants will be aged six to seven-years-old and this is a relatively young age to determine the study objective. The Committee asked if another study will be conducted later for older children. The researcher agreed but noted that many other studies have selected the same age point or younger. Based on the study signals they will be able to determine whether to look at older students. The researcher noted that nine-years-old could be a good age for a later study, however, teenage years would be difficult.
2. The Committed noted that the ‘GiST letter to principals’ document has been separated from the ‘GiST school intro letter’. The Committee asked for clarification about why this was done. The researcher stated that because Principals are very busy the letter to Principals is intended to be short and informative about the study so that they can then delegate tasks to front desk/other staff to help find teachers and rooms to assess the participants.
3. The Committee noted that data may be sent overseas as anonymised research data. The Committee asked if this is optional or a blanket requirement. The researcher stated that the expectations from journals is that the anonymised data will be made available. The Committee confirmed this is fine and that the researcher had made this clear in the Participant Information Sheet.
4. The Committee referred to the peer review obtained for the study. The Committee asked if the researcher considered the reviewers’ comments about the timeline were realistic and asked about the standardisation of assessors. The researcher stated that the study grant is for two years and they have a team of assessors that coordinate and work efficiently, so they consider the timeframe is achievable. The team of assessors are trained and standardised across all study assessments. All assessments are also completed on iPads and laptops.
5. The Committee noted that the children may be living in rental accommodation and moving around a lot and therefore potentially moving between schools. The Committee asked if the researcher will contact children’s previous as well as current schools. The researcher stated that this is not part of the protocol so only current schools and teachers will be contacted.

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 addressed the application for waiver of consent for using the maternal and infant data on the National Women’s Health database to find potential participants. The Committee noted that the researcher’s previous application included more variables on which the match was based on and therefore asked for clarification of what data the waiver was sought for. A significant amount of data was requested in order to find a matched mother (i.e. ethnicity, age, baby’s date of birth, socioeconomic status etc.) The researcher stated that the variables are the same as in the protocol. Further, the researcher referred to practicality and scientific validity in terms of the NEAC Standards. The Committee accepted this but noted and echoed the caution from the researcher’s consumer advisor around how to frame this in the invitation/approach to potential participants. Currently, the language used may be stigmatising in that participants are invited as a comparison group who did not have gestational diabetes. Less stigmatising language to use to outline the comparison could be ‘maternal characteristics’, for example.
2. The Committee noted that the peer reviewer suggested using a verbatim script for the first phone call to parents. The researcher stated that they will provide this to the Committee with the waiver documentation.
3. The Committee noted that the children’s assent form currently could be interpreted as though children could identify themselves in a group where their mother has had too much sugar. The Committee asked the researcher to reframe the information and language used.
4. The Committee asked if the two groups of children will undergo similar assessments. The researcher confirmed that all assessments are the same and will be conducted by the same assessors. The Committee asked if this would contribute to managing the potential stigma for children in the GDM group. The researcher stated that they did not consider there to be any stigma. The children in the pre-hPOD study (a randomised controlled trial in 2013 – 2014 in Auckland maternity hospitals of prophylactic oral dextrose gel in babies at risk of neonatal hypoglycaemia) cohort were already aware that they were at risk of having low sugar levels at the time of being born but that there were multiple reasons for that, including gestational diabetes. The Committee asked if the school will know which group the children are in. The researcher stated that the principal will receive a letter stating whether children were part of the pre-hPOD study. The Principal will not know why the children were part of that study. For the children who are part of the GiST study (the control group), the Principal will be informed that the researcher is looking for children whose mothers did not have gestational diabetes. The Committee considered that the ‘GiST letter to Principals’ document does not accurately capture why the two study groups are being matched. The Committee suggested that the researcher state ‘similar mothers’ for a more general approach to communicate the comparison instead.
5. The Committee referred to the teacher’s questionnaire that will be completed in REDCaP. The Committee noted that the researcher stated this will be anonymous and asked for confirmation that teachers will not put their names on the questionnaire. The researcher confirmed this. The Committee asked if the researcher anticipates that parents may ask for copies of the teacher’s report. The researcher confirmed this. The Committee stated that there needs to be a consent process for teachers. This is to inform teachers that parents may ask for a copy of the report. The Committee requested that the researcher provides a separate consent form for teachers.
6. The Committee noted that the information for schools document states that the researcher will not collect any information from school records, however, this is incorrect. Although school records may not be accessed directly, they will still be accessed through the teachers’ reports. Please amend this statement.
7. The Committee asked if the teachers will complete the questionnaires during school hours or in their personal time. The researcher stated that either option is possible, and they will provide koha to teachers. The Committee noted that Principals may want to be involved in terms of when teachers will complete the questionnaires. The researcher stated that they could provide an estimate of time it will take to complete the questionnaires and include this in the ‘GiST letter to Principals’ document.
8. The Committee asked if it is possible that there will be more than one child participating in the study from each school. The researcher confirmed that this may be possible because the children will have all been born in Auckland in the same hospital. The researcher stated that they may not be able to approach schools about all children at the same time. The Committee requested that the researcher flag this with Principals to advise that they may need to contact them again at another time.
9. The Committee noted that schools may request more information such as police vetting for the research team. The Committee suggested it would be helpful to provide schools with more information about who the researchers are. The researcher also noted that parents have the option to attend the assessments, but it is unlikely that they will.
10. Please provide information to the parents in the ‘GiST Parent Invite letter’ document by stating how parents’ information was obtained and provide them with the option to be removed from the study list and not contacted again.
11. The Committee referred to the Data Management Plan. The Committee noted that this does not mention school records or questionnaires and that it incorrectly states that all participants will give consent. Issues pertaining to data going overseas needs to be improved, as well as in relevant Participant Information Sheets and Consent Forms. Please review and tailor the Data Management Plan specifically to the study and check all other documentation is consistent with it, especially the Participant Information Sheets and Consent Forms.
12. Please clarify what the contact track and tracing involves, especially if it includes home visits 'to collect consent forms', ensuring that the safety of the assessors making the home visits is assured. Please also include a home visit safety plan in the Protocol.

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

1. Please clearly state at the beginning of the document why people are being invited to participate in the study and how their information was obtained.
2. Please provide more information about what the assessments will involve so that children have more detail about what the assessments will be like. For example, it could be helpful to include a photo of a child trying the balance pose.
3. Please provide information about how the iPod Touch will be fitted and worn around the children’s waists. This must be done in an age appropriate way.
4. Please include a tick box in the Consent Form for participants to give permission to the researcher to access their health records and school records.
5. In the Main Parent Participant Information Sheet and Consent Form, please make it clear that it is about the child and the caregivers’ participation. Please include information about what happens in each case i.e. for the caregiver and for the child for all relevant situations, for example, and non-exhaustively, access to medical records, withdrawal from the study, and data privacy sections. Please ensure the consent form includes sections for the caregiver’s participation.

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 2019, 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 Kate Parker and Mrs Kate O’Connor.

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|  **8**   | **Ethics ref:**   | **21/NTA/108** |   |
|   | Title:  | Safety and Effectiveness of Eye90 Microspheres™ in the Treatment of HCC and mCRC |   |
|   | Principal Investigator:  | Associate Professor Andrew Holden |   |
|   | Sponsor:  | ABK Medical Inc. |   |
|   | Clock Start Date:  | 08 July 2021  |   |

Associate Professor Andrew Holden and Helen Knight 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 Study

1. The study is a prospective first in human study to evaluate the effectiveness of radioembolization using Eye90 microspheres in the treatment of patients with unresectable hepatocellular carcinoma and metastatic colorectal carcinoma.
2. The Eye90 device has not been approved for sale or commercial use in any country. Participation will provide data that will help determine whether the study device is safe to use in humans and provide preliminary information as to how well it works. The study will enrol up to 10 patients at Auckland City Hospital, New Zealand.

Summary of resolved ethical issues

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

1. The Committee asked the researchers to clarify whether radioembolization is not available in New Zealand or not available at Auckland District Health Board. The researchers advised that it is available in New Zealand but only through the private system as it has not met approval for government funded treatment in the public system. However, radioembolization is widely used and publicly funded in Australia and overseas.
2. The Committee asked if the study participants will have had a new diagnosis or will they have exhausted all other options. The researchers stated that participants will have exhausted all other options. There are two subsets of potential participants. Patients who have colon cancer and have had that managed but the cancer has moved to their liver only - but they are unable to have resection and are not responding to chemotherapy. The second subset are patients with cancer too advanced for treatments like resection and transplant and their only options are either no treatment or to have radioembolization through the study.
3. The Committee asked if participants will be recruited through referral from the oncology department. The researchers stated that participants would be identified at multidisciplinary meetings. Participants would then be contacted either by phone or in clinic since they will already be due for several appointments. The Committee noted that the Participant Information Sheet makes it clear that there is a screening period for about 35 to 40 days and that participants will be consenting to written information to go into the screening period.
4. The Committee asked if there will be an independent medical reviewer and if they are from New Zealand. The researchers advised that the reviewer is from the United States. There is no other medical practitioner in New Zealand who performs the procedure apart from Associate Professor Holden. The Committee asked if the delivery system for the study is the same as the radioembolization he performs in the private system. He advised that it is similar but some of the technical issues are different so more education is required on his part. An audio-visual link will be set up for proctoring and to practice the procedure. The Committee asked if this will be done before any participants are enrolled. The researchers confirmed that they would not start any enrolment until they are comfortable with the device.
5. The Committee asked if Māori review has been undertaken. The researchers confirmed this and advised that the study was approved with a request for one change to the cultural statement in the Participant Information Sheet.
6. The Committee noted that the insurance policy is for two years and asked if the researchers considered this sufficient. The researchers stated that there will always be an insurance policy for the duration of the study while it is active. Further, the adverse effects of radioembolization are experienced in the first two to three months of treatment.

Summary of outstanding ethical issues

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

1. The Committee noted that the protocol is currently written according to the 2009 NEAC guidelines. Please amend the protocol so it complies with the current *National Ethical Standards for Health and Disability Research and Quality Improvement 2019*.
2. The Committee noted that the data management section of the protocol was incomplete. For example, and non-exhaustively, please provide more information about how images will be de-identified, how data will be transmitted and stored (including protections for images being put on a disc and sent to the United States, what happens to the questionnaires etc. This section must cover all types of data being collected for the study. If the protocol includes sufficient detail about data management, it will not be necessary to provide a separate Data Management Plan. Please refer to the [HDEC template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/data-only-management-template-oct2020.docx) for guidance on what a Data Management Plan should include. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15a).*
3. The Committee referred to the table under the ‘Screening’ section of the Participant Information Sheet. The potential participants do not have other viable treatment options, so the table is not likely to be helpful. The Committee requested instead that the researchers inform potential participants what they will undergo as part of the study and that it will be funded, rather than compare to standard care that cannot be provided to them currently. In doing this, please provide reassurance that potential participants will still get the clinic visits that they would ordinarily get. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.19).*
4. The Committee asked the researchers to explain the microspheres and what makes them visible in real time because there is no information in the study documentation about the elements themselves which make the microspheres radio-opaque. The researchers stated that the microspheres have a radio-opaque lining and outlined the process of how the microspheres are delivered to the target. Please include information about what it is that makes the microspheres radio-opaque in the Participant Information Sheet and study documentation. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.19).*
5. The Committee also noted there is no information in the study documentation about whether the radio-opaque elements inserted in the microspheres have the potential to leak.
6. The Committee noted that there were some pre-clinical trials on animals that had not been completed at the date the Protocol was written in June 2021. Please provide this information and include it in the study documentation. Please also provide evidence that the peer reviewer has reviewed the results of any pre-clinical trials on animals. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.25).*
7. The Committee noted that the Participant Information Sheet refers to filming the procedure. The Committee asked the researchers to explain this and confirm whether it is optional. The researchers stated that the procedure will be livestreamed for the sponsor and that this is compulsory. The procedure will not be recorded and stored. The Committee asked the researchers to replace any wording around the procedure being ‘filmed’ with ‘livestreamed’. Please also remove the tick box in the Consent Form about the sponsor being present for case support during the procedure as the researchers advised that this is required and not optional. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.19).*
8. Please ensure that the Participant Information Sheet and Consent Form complies with the Health Information Privacy Code 2020 and Privacy Act 2020. Please note that there is a new right under the Privacy Act 2020 about data being sent overseas and there are warning statements that must be included for this – refer also to the [*National Ethical Standards for Health and Disability Research and Quality Improvement 2019*](https://neac.health.govt.nz/national-ethical-standards/part-two/12-health-data/).
9. Please provide the risk analysis referred to in the Protocol that evaluated the use of Eye90 microspheres for the treatment of malignant hyper-vascular hepatic neoplasia.

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

1. Please refer to the correct HDEC on pages 9 and 11 (Northern A HDEC).
2. Please do not introduce new information in the Consent Form that is not in the body of the Participant Information Sheet. For example, and non-exhaustively, advising participants’ general practitioners of participation in the study is only mentioned in the Consent Form and not explained.
3. Please categorise the list of side effects by ‘severity’ instead of ‘type’.
4. Please include the additional risks that are currently only mentioned in the Investigator’s Brochure, in order to obtain fully obtained consent.
5. Please quantify the statement that says the risk of migration of radiation beads is low.
6. Please expand on the risks of angiogram and make it clear that it is only for the research.
7. Please review whether the ‘alternative treatment’ section is correct and should be included.
8. Please mention the potential for data to be used for future unspecified research (if this will be done). Please ensure the documentation complies with para 7.57 of the [*National Ethical Standards for Health and Disability Research and Quality Improvement 2019*](https://neac.health.govt.nz/national-ethical-standards/part-two/7-informed-consent/) and get participants’ consent for this.
9. Please improve the data section and refer to the [HDEC template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc) for assistance. For example, and non-exhaustively, please provide more detail about the place where the medical imaging will be sent overseas and include a fuller statement about risks of data going overseas, especially having regard to the requirements of the Health Information Privacy Code 2020.
10. Please expand on the ‘incidental findings’ section on page 8 and explain what those might be.

Decision

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

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|  **9**   | **Ethics ref:**   | **21/NTA/114**  |   |
|   | Title:  | Doxycycline after sinus surgery  |   |
|   | Principal Investigator:  | Dr Andrew Wood  |   |
|   | Sponsor:  |   |   |
|   | Clock Start Date:  | 08 July 2021  |   |

Dr Andrew Wood 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 Study

1. This is a randomised double blinded placebo-controlled study. The study will include patients undergoing Endoscopic Sinus Surgery (ESS) for sinusitis in various Public Hospitals across the North Island of New Zealand. The researchers plan to recruit a total of 50 patients. The researchers are studying the use of antibiotics (doxycycline) to see whether they make improvements after surgery or whether they cause side-effects and complications.
2. Participants will be randomly allocated to receive either doxycycline or placebo tablets.
3. Except for being provided either antibiotic tablets or placebo tablets after surgery, clinical care including the details of the operation and the care after surgery will be exactly the same. There will be no further visits to the hospital required beyond normal care.
4. When participants attend for surgery and the clinic visits after surgery, the researchers will collect information about the severity of sinusitis including the severity of symptoms as well as taking samples of mucus from the nose and sinuses to assess the effect of the tablets on the bacteria and inflammation that is present.

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 it is not yet known whether antibiotics after surgery is good. The researcher stated it has not been properly studied yet. When surveyed, 73 percent of surgeons reported they gave courses of antibiotics after surgery because it apparently does not cause harm. However, the researcher considers that there may be no benefit to it, or there may be a trend towards it making recovery after surgery worse. Accordingly, the study aims to demonstrate that it is inferior to use a course of antibiotics after endoscopic surgery.
2. The Committee asked if doxycycline is the default antibiotic. The researcher stated that it is one of the defaults as it also has good coverage and is not resistant to
staphylococcus aureus. There is limited data on the primary treatment of sinusitis with doxycycline and poor evidence for any other antibiotic, hence why the researcher chose doxycycline for the study. The Committee asked if the study is still in equipoise and the researcher confirmed this.
3. The Committee noted that Clinical Trials New Zealand is mentioned with the study sites. The researcher clarified that there are four potential study sites: Auckland Hospital, North Shore Hospital, Waikato Hospital, and Wellington Hospital. Clinical Trials New Zealand will be providing support only for Waikato Hospital (where the researcher is based). The statement that documents will be stored at a clinical trials agency during the study is only in relation to Clinical Trials New Zealand and participants in Waikato.
4. The Committee advised that it normally would not accept investigators as experts undertaking their own study peer review. However, the Committee was satisfied for this study and agreed it would not request independent peer review as it is not concerned about the scientific validity for this study.

Summary of outstanding ethical issues

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

1. The Committee noted that there is variation in standard of care and asked the researcher to include this information in the Participant Information Sheet.
2. The Committee noted that there was no description in the Protocol or Participant Information Sheet about how side effects will be measured. Given that this is one of the study outcome measures, please provide more information in the Protocol about how this will be done.
3. The Committee referred to the Data and Tissue Management Plan (DTMP) and noted that information about the study data was not clear and referred to identifiable information. The Committee also noted that Case Report Forms (CRFs) are mentioned but there is no description as to whether they are electronic or paper based. The researcher stated that the CRFs will primarily be paper based. The study data is de-identified and stored at each study site. Please put a study code on the CRFs and ensure there is no identifiable information. Please also do this for tissue samples and ensure that the samples are not labelled with identifiers (page 5 of the DTMP).
4. The Committee noted that the procedure will be videoed and requested clarification about how the videos will be used. The researcher stated that the videos are recorded on site for the two follow up consultations and is standard care. The videos are required in order to draw an endoscopic score. Please include information about the videos in the DTMP.
5. The Committee noted that the DTMP refers to future unspecified research. Please ensure that there are sufficient overseas warning statements for the future unspecified research section and in the Participant Information Sheet. This is required to comply with the Health Information Privacy Code 2020 and Privacy Act 2020. There is a new right under the Privacy Act 2020 about data being sent overseas and there are warning statements that must be included for this. Please also refer to the [*National Ethical Standards for Health and Disability Research and Quality Improvement 2019*](https://neac.health.govt.nz/national-ethical-standards/part-two/12-health-data/).
6. The Committee referred to page 4 of the Participant Information Sheet and noted that there is information missing about who will be funding the study. The researcher advised that the study will be grant funded, but applications do not open until August 2021, so they are preparing in advance. Please provide this information once it is available.

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

1. Please mention the pilot study and include the quantified data in regards to the 73 percent of surgeons administering a course of antibiotics after surgery as noted above.
2. Please provide detail about the procedures around taking doxycycline. For example, more information is required to inform participants that they will take an oral tablet, how many times per day it must be taken, and over how many days.
3. Please provide information about the side effects the study will look at.
4. Please provide more information about the risks for participants in the placebo arm (such as post-operative infection) and also for participants in the control arm of the study.
5. Please include information about the types of information that will be accessed from participants’ medical records. Please also include a tick box in the Consent Form confirming participants agree to this.

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 Karen Bartholomew and Ms Rochelle Style.

## General business

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

|  |  |
| --- | --- |
| **Meeting date:** | 17 August 2021 |
| **Meeting venue:** | Online via Zoom |

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**

The Committee discussed a complaint that had been received in relation to a study it had previously considered. The Committee was made aware of the complaint prior to the meeting. The Chair outlined the process and confirmed the Committee’s role would be to look at the study again when the researchers provided a response to the Committee.

1. **Other business for information**
2. **Any other business**

The meeting closed at 6.10pm.