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| **Committee:** | Northern B Health and Disability Ethics Committee |
| **Meeting date:** | 06 April 2021 |
| **Meeting venue:** | ONLINE - Zoom Meeting |

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| **Time** | **Item of business** |
| 12:00pm | Welcome |
| 12:25pm | Confirmation of minutes of meeting of 02 March 2021 |
| 12:30pm | New applications (see over for details) |
| 12.30pm  12:55pm  1:20pm  1:45pm  2:10pm  2:30pm  2:55pm  3:25pm  3:45pm | i 21/NTB/73 Susan/Stephanie  ii 21/NTB/69 Tangihaere/Jane W  iii 21/NTB/70 Kate/Stephanie  iv 21/NTB/71 Susan/Jane W  *Break (20 mins)*  v 21/NTB/72 Tangihaere/Jane W  vi 21/NTB/63 Kate/Stephanie  vii 21/NTB/75 Susan/Jane W  viii 21/NTB/74 Kate/Stephanie |
|  | General business:   * Noting section |
| 4.00pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Mrs Stephanie Pollard | Non-lay (intervention studies) | 01/07/2015 | 01/07/2018 | Present |
| Miss Tangihaere Macfarlane | Lay (consumer/community perspectives) | 20/05/2017 | 20/05/2020 | Present |
| Mrs Kate O'Connor | Lay (ethical/moral reasoning) | 14/12/2015 | 14/12/2018 | Present |
| Mrs Leesa Russell | Non-lay (intervention studies), Non-lay (observational studies) | 14/12/2015 | 14/12/2018 | Apologies |
| Mr John Hancock | Lay (the law) | 14/12/2015 | 14/12/2018 | Apologies |
| Mrs Jane Wylie | Non-lay (intervention studies) | 20/05/2017 | 20/05/2020 | Present |
| Ms Susan Sherrard | Lay (consumer/community perspectives) | 19/03/2019 | 19/03/2022 | Present |

## Welcome

The Chair opened the meeting at 12:00pm and welcomed Committee members, noting that apologies had been received from Mrs Leesa Russell and Mr John Hancock.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

The Chair provided a verbal update on the 30 March HDEC Chairs Day.

## Confirmation of previous minutes

The minutes of the meeting of 2 March 2021 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **21/NTB/73** |
|  | Title: | PCOL-102-AHSF\_ATHENA Study |
|  | Principal Investigator: | Dr Dean Corbett |
|  | Sponsor: | Johnson & Johnson Surgical Vision, Inc. |
|  | Clock Start Date: | 25 March 2021 |

Dean Corbett 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.

Stephanie Pollard declared a potential conflict of interest and was excused from discussion. The Committee noted that the declaration also applies to the previous (active) study, 19/NTB/196.

Summary of Study

1. The study will test two new intraocular lenses. It is a multicenter, prospective, randomized, subject-and-evaluator-masked, bilateral-implant study. The study will be conducted at up to 15 sites worldwide with 25 New Zealand participants.

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 the market cost of cataract lenses and asked if there was a potential cost-saving advantage for participants in this study. The researcher confirmed there is, particularly as these lenses are not covered by government funded medical insurance in New Zealand.
2. The Committee queried if producing a receipt for travel reimbursement would be onerous for participants. E.g. for reimbursement of petrol when travelling by car. The researcher advised that in these instances, they would make an estimate of the cost of petrol or taxi rides and provide an MTA voucher as compensation.
3. The researcher also confirmed that he will ensure the expense amounts that can be claimed are comparable across the country.
4. The Committee asked why the sponsor is only covering travel costs for 3 of the 8 visits. The researcher stated they were unsure and would confirm with the sponsor.
5. The Committee noted that the participant information sheet mentions the sponsor stopping the study for any reason and informed the researcher that in New Zealand you cannot terminate a therapeutic study for commercial reasons only. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.37).*
6. The Committee recommended that when answering the benefit to Māori question (p.4.1), to start with an explanation of the incidence of the disease in Māori, including any statistics to support this. Please bear this in mind for future applications.

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

1. Please amend the statement on page 3 to include the word “clinical” as follows; "You can’t be in this study if you were in another clinical study within 60 days of the first visit of this study".
2. Please amend the ‘Will any costs be reimbursed’ section to cover travel costs for all visits.
3. Please reword the statement “JJSV may also stop the study at any time for reasons they decide to be appropriate” as studies may not be terminated for commercial reasons in New Zealand.
4. Please remove the reference to Medicines NZ guidelines from the compensation section as these guidelines do not apply to devices.
5. Please provide a fuller explanation of what the additional visual testing is and what, if any, additional discomfort the testing may cause.
6. Please add a statement acknowledging the taonga status of Māori data under the ‘What happens to my information’ section.

Decision

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

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

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| **2** | **Ethics ref:** | **21/NTB/69** |
|  | Title: | Phase 2b Safety and Efficacy Study of REN001 in Mitochondrial Myopathy |
|  | Principal Investigator: | Dr Richard Roxburgh |
|  | Sponsor: | Neuroscience Trials (NTA) AUS |
|  | Clock Start Date: | 18 March 2021 |

Kay Yeoman and Miriam Rodrigues and Annie Bradley 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 trials a new drug treating Mitochondrial Myopathy. It is a double-blind, placebo-controlled, study to evaluate the efficacy and safety of treatment with REN001 over 6 months. It is a global study with 200 participants of which five 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 Committee queried if gene testing for mitochondrial DNA mutation will be done locally or sent away to a central laboratory. The researcher advised that as they are recruiting people who have been identified as having the condition and therefore the participants will already have had the gene testing through standard of care.
2. The Committee queried why the participant documentation states that there is no ongoing provision for the study drug after the participants complete the study, however the protocol mentions an open label extension study. The researcher advised that while they are hopeful there will be an extension study, they do not want to offer it to participants during consent process as it might not happen.
3. The Committee asked what provision there is for people who do not have a smart phone or internet to meaningfully engage in the study. The researcher advised that they will investigate how they can make this work using paper copies for non-digital participants.
4. The Committee queried what tikanga protocols are in place for home visits. The researcher advised that they will only be conducting home visits as a back-up plan in the event of Covid-19 restrictions for example.
5. The Committee recommended that when answering the benefit to Māori question (p.4.1), to start with an explanation of any disproportionate burden to Māori from the disease including any statistics to support this. Please bear this in mind for future applications.
6. The Committee stated that relevant Māori cultural issues for this research (p.4.2) would include the taking, transporting, storing and disposing of tissue samples as tapu, and acknowledging the taonga status of data. Please bear this in mind for future applications.
7. The Committee asked if the urine samples will be sent overseas. The researcher responded that, while they are not 100% sure yet, it is highly likely they will be sent overseas.

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 travel expense reimbursement system appeared quite complex. The researcher advised that using a third-party vendor to book travel/reimburse expenses usually works well for all involved. She added, however that vendors have pulled out at the last minute and that while there is the possibility of using third-party vendors in this study, they may not have control over it.
2. The researcher advised that to ease the burden of reimbursement on participants, they intend to book and pay for as much travel/flights for participants up front.
3. The Committee was concerned over the lack of transparency of third-party vendors’ access to participants’ personal information and how it will be used (i.e. travel app, pedometer, etc). For example, the privacy policy for patientprimary/Primarius (concierge expenses reimbursement service) allows it broad rights to use and share participants’ data, including after they have withdrawn.
4. The Committee stated that this is not in the participants best interests and it must be managed and clearly communicated to participants to ensure informed consent. Please update the data management plan to detail how the protection of participants data/privacy will be managed with respect to third party vendors.
5. The Committee noted that the participant information sheet and consent form (PIS/CF) states that using the concierge expenses reimbursement service is optional. The Committee requested clarity on what other (less onerous and non-digital) alternatives for expenses reimbursement are available.

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

1. Please include the number of participants involved in previous trials on page 2.
2. Please mention that the participants will be allocated to a group by chance under the ‘How is the study designed’ section on page 3.
3. In the paragraph about tumours in animals, please add one of these statements – whichever is correct; “there has been no studies in humans to date” or “there is no information on the cancer-causing effects in humans to date (page 3).
4. Please update the ‘What will happen to my information” section to include more information on the identifiable data that the third parties will hold about the participants as per the ethical issue raised by the Committee above.
5. Please remove the yes/no tick boxes for optional items from the consent form unless they are truly optional.
6. Please amend statement from “discuss these concerns with a kaumatua or whanau member” to “discuss with someone you trust” on page 5.
7. Please indicate whether there will be opportunity for karakia at time of tissue disposal.
8. Please provide an explanation of “bone marker” that is referenced on page 4.
9. Please amend the bullet point “Be willing and able to swallow gelatine capsules” to “Be willing and able to swallow capsules, including gelatine” on page 5.
10. Please add a statement acknowledging the taonga status of Māori data under the ‘What happens to my information’ section.
11. Please include a cultural tissue statement on page 9. The Committee recommended the following statement as a guide: “You may hold beliefs about a sacred and shared value of all or any tissue samples removed. The cultural issues associated with sending your samples overseas and/or storing your tissue should be discussed with your family/ whānau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult before participating in research where this occurs. However, it is acknowledged that individuals have the right to choose.”
12. In the Welcome letter, please include a contingency for home visits.
13. In the Patient Urine Collection PIS/CF, please consider alternative wording for “entire void” that will ensure participants understand what you mean.

Decision

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

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

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| **3** | **Ethics ref:** | **21/NTB/70** |
|  | Title: | Study of Encorafenib and Binimetinib Plus Pembrolizumab in BRAF V600E/K Mutation-Positive Metastatic or Unresectable Locally Advanced Melanoma |
|  | Principal Investigator: | Dr Gareth Rivalland |
|  | Sponsor: | Pfizer Australia |
|  | Clock Start Date: | 25 March 2021 |

Amy Tong and Gareth Rivalland 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 compare the efficacy of encorafenib and binimetinib plus pembrolizumab (TRIPLET) versus placebo plus pembrolizumab (CONTROL) in participants with metastatic or unresectable locally advanced BRAF V600E/K-mutant melanoma.
2. New Zealand will not participate in the safety lead in phase and will only be involved in phase 3, where participants will be randomized in a 1:1 ratio to the Triplet Arm or Control Arm. There will be 10 NZ participants and16 countries involved in this phase of the study.

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 an amendment to the Investigators Brochure for Pembrolizumab (Pembro) was recently submitted (version 20) and recommended the researchers ensure they are working to the later version to address all the identified risks
2. The Committee asked what funded treatment options are available in New Zealand for this type of cancer and if there were any disadvantages to participating in this trial such as missing out on the alternative (funded) standard of care treatments.
3. The researcher stated that the only funded, meaningful treatment available to people with this form of mutated melanoma is Pembro. He added that there are no known disadvantages as the duration of the trial treatment in is line with standard of care treatment of two years and these participants would likely still qualify for the funded standard of care.
4. The Committee advised that pregnancy information sheets are typically submitted for review in the event of a participant or partner pregnancy and are not required upfront.
5. The Committee noted the researcher confirmed that CYP3A4 inhibitors are excluded in phase 3 as well as the safety lead in.

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 application (question p3.3.1) is missing detailed information on the types of expenses that will be reimbursed and the maximum amounts. It is also missing the process for requesting approval for expenses in excess of the standard amount. Please provide this information to participants so they understand they will not be out of pocket if they join the study.
2. The Committee recommended that the value of expenses offered should be comparable across the country to ensure equity in participant reimbursement.
3. The Committee recommended that the emergency card includes a local New Zealand phone number under the Secondary Emergency Contact instead of a website link. This is to make it easy for the caller to get in contact with the sponsor quickly when required.
4. The Committee noted that there is a substantial amount of information for participants to digest upfront in the Main PIS/CF that could lead to confusion about what is optional and what is not when consenting. They stated that consenting is an ongoing process and is best spaced out with consent obtained at the most appropriate time to allow for optimal understanding.
5. The Committee recommended mandatory information for the main study (and related consent) be on a separate PIS/CF to distinguish it from optional elements.
6. The Committee recommended gaining consent for the optional research as and when needed. For example, consent for the optional biopsy is not required at the beginning of the study and could be delayed. The researcher confirmed they will discuss this with the sponsor.
7. The Committee asked whether consent in the pregnancy form is for the disclosure of health information for the infant after birth or if it is for in utero only. The researcher confirmed that they require in utero information only and nothing after birth. The Committee recommended removing the references to the infant’s data and outcome of birth.
8. The Committee advised that the mother, even a minor, is legally authorised to consent for their baby and therefore the minor consent section referencing the father and maternal grandfather is not required.
9. The Committee noted there is little information in the PIS/CF on prohibited medications and asked what these are in the study. The researcher stated that the use of CYP3A4 inhibitors, anti-fungals, live vaccines (e.g. measles mumps, yellow fever, shingles) are prohibited; however, the flu and Covid-19 vaccines are not prohibited. Please include more information in the PIS/CF.
10. The Committee noted that the optional biopsy PIS/CF states that results 'may or may not be shared with doctor'. The Committee asked which, if any, genetic testing results will be disclosed to the participants’ doctors. The researcher confirmed that only test results directly related to the trial, and none of the optional research test results, will be shared with the New Zealand research team and then provided to the participant’s doctor.
11. The Committee advised that where research generates information of potential importance to the future health of participants or their family/relatives, researchers must flag the existence of and use of the information according to a detailed protocol *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 14.37).*
12. The Committee acknowledged ambiguity around whether this specific ethical obligation also applies to international research teams on the study. They recommended this is discussed with the sponsor and consideration given to how they plan to address this ethical standard with the future research testing results being withheld overseas.
13. The Committee asked if Merk will be receiving any study data? The researcher advised that the study is in collaboration with Merk and it is highly likely they will receive study data. Please update the data management plan accordingly.
14. The Committee noted that you intend to still use samples from participants who do not make it beyond the screening process in the study. This seems unusual as the purpose of the samples is in response to treatment they’re receiving, unless it is for future research. Please clarify this.

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

*All PIS/CFs*

1. Please ensure all PIS/CF statements are tailored to their individual content rather than replicating main PIS/CF. E.g. BRAF form needs to state that the intervention is not proven to be effective in this population.
2. Please provide a thorough proofread of PIS/CFs for grammar and spelling mistakes.
3. Please clarify sponsor(s) on the front-page headers. Currently it is identified as Pfizer but there is reference of samples going to a sponsor biobank in the US and the study is being done in collaboration with the pharmaceutical company, Merk.
4. Please ensure the data management section includes all companies accessing participant data (e.g. Merck).
5. Please ensure inclusion of the contact details for Māori health/cultural support person.
6. Under the ‘What happens to my samples?’ section, please state if there will be an opportunity for karakia at time of tissue disposal and include a cultural statement on tissue sample collection. The Committee recommended the following statement as a guide: “You may hold beliefs about a sacred and shared value of all or any tissue samples removed. The cultural issues associated with sending your samples overseas and/or storing your tissue should be discussed with your family/ whānau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult before participating in research where this occurs. However, it is acknowledged that individuals have the right to choose.”
7. Please also state whether there will be an opportunity for karakia at time of tissue disposal.
8. Please include statement acknowledging taonga status of Māori data under the ‘What will happen to my information?’ section.

*Main PIS/CF*

1. Please update the statement “Your study doctor will discuss these with you” when referring to prohibited medication to something like “if you are taking medication or are planning a vaccination, please discuss these with your study doctor”.
2. Please update the ‘What are the alternatives to participation?’ section to more accurately explain what alternative treatments are truly available in New Zealand (page 21). E.g. state whether a drug is approved but not funded in New Zealand.
3. Please detail what types of expenses will be reimbursed and the amounts (e.g. “to the maximum of…”)
4. Please include a statement on the process for reimbursement of costs outside the standard rate. E.g. “In the case of an unusual event (like high travel costs) or unscheduled visits, expenses of more than $xx may be reimbursed with approval from the Sponsor.”
5. Please write FDA out in full on Page 2.
6. Please amend the wording from ‘you may be reimbursed’ to “you will be reimbursed up to…” on page 2.
7. For banked biospecimen, please ensure this form acknowledges the optional nature of this blood collection on pages 6 and 12.

*FUR PIS/CF*

1. Please ensure page 12 and 14 have a consistent duration for the length of time biospecimens will be banked for (e.g. indefinitely vs 15 year).
2. Please clearly outline the specific reporting requirements for HIV and hepatitis in New Zealand on page 4.
3. On page 3, under the ‘What happens to my samples?’ section, please state if there will be an opportunity for karakia at time of tissue disposal and include a cultural statement on tissue sample collection.
4. Please include statement acknowledging taonga status of Māori data.
5. On page 2, it is unclear as to whether the combination is approved by the FDA or not. Please clarify and add the status of Pembro and other drugs available in New Zealand.
6. Please make it clear whether any information/results from genetic testing that may impact participants and their relatives will be shared with them or their doctors – as per point discussed by Committee above.

Decision

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

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

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| **4** | **Ethics ref:** | **21/NTB/71** |
|  | Title: | ANX007-GA-01: A Study Investigating the Efficacy and Safety of Intravitreal Injections of ANX007 in Patients with Geographic Atrophy (ARCHER) |
|  | Principal Investigator: | Dr Oliver Comyn |
|  | Sponsor: | Annexon Biosciences, Inc. |
|  | Clock Start Date: | 25 March 2021 |

Oliver Comyn, Sharon Turner, Lori Taylor, W Murahashi, Harman Hansra 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 testing a new medicine for treatment of geographic atrophy. A phase 2, multicentre, randomised, double-masked, sham-controlled study of intravitreal injections of ANX007". Approximately 240 participants with 15 in New Zealand and will be randomly assigned to one of four treatment arms.

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 what the degree of risk is of developing wet macular degeneration from receiving the study molecule. The researcher stated that he does not have data to date but will be evaluating this in the study.
2. The Committee asked what the available treatments for managing wet macular degeneration are and the success rate of them. The researcher stated that if wet macular degeneration is caught early, there is 90% chance of stabilising the condition and preventing further loss of vision as well as potentially reversing some of the damage with treatment. He added that as the participants will receive a high level of monitoring during the study, they are confident they will catch any occurrences of the condition early.
3. The Committee queried if there are alterative syringes to BD syringe, which has reported side effects, that can be used in the study. The sponsor advised that because of the requirement for a luer lock syringe and the compatibility with their drug, the BD syringe is the only syringe they can use in the study. The sponsor and researcher advised that they have not experienced any of the reported side effects in the several years they have been using the syringes.
4. The Committee reminded the researcher that his Medical Protection Society certificate needs renewing.
5. The Committee recommended that when answering the benefit to Māori question (p.4.1), to start with an explanation of incidence of the disease in Māori, including any statistics to support this. Please bear this in mind for future applications.
6. The Committee advised the researcher that relevant Māori cultural issues for this research would include taking, transporting, storing and disposing of tissue samples and in this case, the tapu nature of the head should also be acknowledged (p.4.2). The Committee requested the researcher become familiar with these concepts and be mindful of this for future applications.

Summary of outstanding ethical issues

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

1. The Committee stated that questions b.1.1 and b.1.2 appear to be missing the word ‘other’ from the sentences, e.g. “once monthly or once every month for 12 months.” Please amend the sentences so they make sense.
2. The Committee advised that as there are substantial changes required to the study documentation, these will need to come back to the HDEC for review.

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

*Main PIS/CF*

1. Please amend the page number typo in the footers.
2. Please add emergency contact number on page 9.
3. Please be clear about where the New Zealand samples will be sent for testing on page 14 (e.g. study samples sent to Australian sonic labs and future unspecified research samples will go to the US).
4. Please remove consent form for withdrawal of participation (or make it option) as written requests are not a requirement in New Zealand and participants can indicate verbally that they wish to withdraw.
5. The sponsor is referred to as Novatech NZ but on page 18 there is reference to ownership rights belonging to Axon Inc. Please clarify who the sponsors are on the front-page header and include the addresses.
6. Please amend the statement “discuss these concerns with a kaumatua or whanau member” to “discuss with someone you trust" on page 14.
7. Please acknowledge taonga status of Māori data (as per Māori Data and Tissue Sovereignty section of Tissue Management Plan). Please also confirm whether or not there will be no opportunity for karakia where tissue disposal occurs overseas.
8. Please ensure inclusion of Māori health/cultural support person details on the contacts page.
9. Please change “visual disability” to “visual impairment” on page 2.
10. Please change blue text to black as it is hard to read and consider making large print copies of the forms available.
11. Please change emergency contact number from "000" to “111” on pages 9 and 13.
12. Please provide an explanation of what "sham" means on page 3.

*Pregnancy PIS/CF*

1. The Committee advised that a separate pregnancy (outcome) consent form will need to be signed by the baby’s guardian if the research team intend to collect data after the baby is born.

*Optional Genetic PIS/CF*

1. Please remove all bullet points in the optional genetic research form that relate to the main study (e.g. collecting and processing health information). Keep points 1-5 and 9 regarding genetic testing.
2. On the consent form, please remove the end of the sentence that says “unless I consent to their storage for future unspecified research” on bullet point about blood samples.
3. Please amend bullet point 9 in the consent form to state “I agree to my blood sample being sent overseas and to be used for genetic research. I am aware that these samples will be disposed of using established guidelines for discarding biohazard waste”.
4. Please replace the generic insurance statement with one that is specific to the study (e.g. include the trial name and reference the specific protocol number in the insurance form.
5. Please amend cultural statement from “discuss these concerns with a kaumatua or whanau member’ to “discuss with someone you trust".
6. Please acknowledge taonga status of Māori data.
7. Please ensure inclusion of Māori health/cultural support person details on the contacts page.
8. Please change blue text to black as it is hard to read and consider making large print copies available.
9. Please amend clause 15 to “This clinical research study is being conducted and funded by Annexon Inc and sponsored by Novotech (Australia) Pty Ltd and Novatech NZ Ltd” or whatever is correct.

Decision

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

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

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| **5** | **Ethics ref:** | **21/NTB/72** |
|  | Title: | Neonate Stoma Refeeding Device Study |
|  | Principal Investigator: | Mr Andre Modesto |
|  | Sponsor: | The University of Auckland |
|  | Clock Start Date: | 25 March 2021 |

Andre Modesto and Greg O’Grady 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. This PhD study will test the feasibility of a neonate stoma refeeding device for neonatal intestinal failure. There will be 20 New Zealand participants.

Summary of resolved ethical issues

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

1. The Committee noted that the study was previously declined as there were several issues with the documentation supplied which appear to have been addressed as per the previous Committee’s request.
2. The Committee stated that they have not reviewed the Nurse participant information sheet and consent form.

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 adult version of the device, manufactured by The Insides Company is commercially available in Europe and New Zealand and asked if any modifications are being made to the device to make it suitable for babies. The researcher responded that the neonatal device needs to be made much simpler than the adult device and requires a different valve.
2. The researcher confirmed that the IP will be linked to the design of the valve but that they are not yet sure if it is novel enough to be patented.
3. The Committee stated that there are significant issues with this application, including the failure to identify it as a commercial study and to disclose the conflict of interest of Greg O’Grady and Ian Bissett as shareholders in the medical device company, The Insides Company, that supplies the refeeding medical devices to Europe and New Zealand. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.23).*
4. The investigator Greg O’Grady confirmed that while the principle shareholder and sponsor is the University of Auckland (UoA), he and Ian Bisset are co-founders/shareholders in The Insides Company. Professor O’Grady stated that failure to disclose this conflict of interest in the application was an oversight and that they plan to correct this.
5. The Committee advised that as The Insides Company is the principal commercial beneficiary of the research, it should be identified as the sponsor rather than UoA. The Committee added that as it is a commercial study compensation is to be covered by the device company’s clinical trials insurance as required under the ACC Act.
6. The Committee asked how the researchers plan to manage Professor O’Grady’s and Ian Bissett’s conflict considering their dual roles as academic supervisors to the PhD student/ principle investigator and shareholders in the device company that will benefit from the student’s research.
7. The researcher advised that Greg O’Grady and Ian Bissett will not be involved in the data analysis stage and have identified their conflict of interest to Uniservices who manage product commercialisation. He added that there is a third supervisor without a conflict that can assist the PhD student with the research project, and they can utilise the UoA statistics department also.
8. The Committee stated that this information is missing from the application and needs to be presented to the HDEC for review.
9. The Committee sought clarity on the physical data that will be collected as the application form states "no tissue", yet the protocol states "laboratory exams." The researchers stated that they will be testing participants for malnutrition using standard of care blood and urine samples and will not be collecting tissue samples.
10. The Committee advised that anything from the body (e.g. urine saliva, blood) is classified as human tissue as per the Human Tissue Act. The Committed stated that the researchers have failed to recognise the use of standard of care blood and other human samples in their application and to disclose it to participants as part of informed consent. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15).*
11. The Committee recommended a tissue management plan based on standard of care assessment to be added to the study protocol and the information sheet updated accordingly. For guidance, please refer to [the HDEC tissue and data management template.](https://ethics.health.govt.nz/updates/new-templates-datatissue-management-plans)
12. The Committee stated that an investigators brochure is missing, and one will need to be submitted to HDEC for review.
13. The Committee noted that the data management plan references some tertiary legislation but does not mention the UoA’s data management policies. The Committee recommended the data and tissue management plan is strengthened to include the information mentioned above once the researchers have accounted for the human tissue data collection.
14. The committee requested that the international databank referenced in section 8.6 needs to be identified and governance documentation provided for it.
15. The Committee requested that the Māori consultation feedback received through Starship is provided to HDEC for review.
16. The Committee advised that it is an HDEC requirement to provide a Universal Trial Number (UTN) in absence of Australian New Zealand Clinical Trials Registry number.
17. The Committee concluded that this application will be declined as it fails to meet several ethical standards and New Zealand legislation. They recommended that the researchers resubmit the application to Northern B Committee ensuring the following information is included:
    * Please address all outstanding ethical issues, providing the information requested by the Committee.
    * Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
    * Please 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).*

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

1. Please replace the ACC compensation statement with the commercial compensation statement.
2. The form eludes to parents authorising information to be shared to researchers on page 3. Please be more specific and include the intention to use the routine laboratory results from their monitoring.
3. Page 5 eludes to potential sharing of information with de-identified data in future. Please be more specific.
4. Please remove additional interpreter boxes and include it once up the front underneath primary contacts and remove it the consent form.
5. Please update the statement under the benefits section on page 4, “This type of treatment has been used in patients previously” to “This type of treatment has been used in children and infants previously”.
6. Please proofread the forms to correct grammatical and spelling mistakes.

Decision

This application was *declined* by consensus, as the Committee did not consider that the study meets the National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15-12.17, 11.23-11.24, 17.1-17.6.

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| **6** | **Ethics ref:** | **21/NTB/63** |
|  | Title: | VEMA - Very Early Medical Abortion Trial |
|  | Principal Investigator: | Dr Gillian Gibson |
|  | Sponsor: | Auckland District Health Board |
|  | Clock Start Date: | 12 March 2021 |

Gillian Gibson 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 will test if the Very Early Medical Abortion (before a pregnancy is visible on ultrasound scan) is as effective as current standard (delayed) early medical abortion (EMA). This is a global study with 100 New Zealand participants.

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 this application could have gone through the Expedited review pathway, however due to the sensitive nature of the study, the Committee considered a full review was warranted.
2. The Committee asked if the VEMA procedure is available in New Zealand outside the study? Researcher stated that she is not away that it is being offered in New Zealand (as a publicly available procedure) but that there is a possibility that it is being offered in the private sector.
3. The Committed agreed that non-inferiority design is appropriate for this study.
4. The Committee asked for explanation of how the study works in lay terms. The researcher advised that the aim is to demonstrate there are no disadvantages to the VEMA treatment option – compared to standard of care options – and if there are potential psychological benefits.
5. The Committee asked how they will measure success? The researcher responded that the patient will complete a short questionnaire to complete over the phone just prior to 4 weeks (end of study) to benchmark with other study sites. She added that the study site will be at Epsom Day Unit, Auckland Hospital, however, results will be combined with findings from other international sites coordinated by the lead site Karolinska Institute in Sweden.
6. The Committee queried if providing questionnaire at week four may be too late for recollection of experience. The researcher advised that the treatment takes two weeks to complete and often patients are still experiencing symptoms. The researcher advised that they are in touch with participants the following day after the procedure, 3 days later and a week later
7. The Committed noted that the peer reviewer states vaginal medication may be a barrier to participation and is not standard of care in New Zealand. The Committee advised that if it is different to standard of care in New Zealand, then the participants will need to be advised. The researcher confirmed that they have agreed with the Sweden study that they can use New Zealand standard of care medication.
8. The Committee noted that the recent legislation changes allow a woman to self-refer to an abortion service provider.

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 if there is any evidence of women changing their minds about an abortion after the ultrasound and seeing a visual. The researcher responded that most women opt out of viewing the ultrasound and it is very rare for anyone to change their minds leading up to an abortion.
2. The researcher further advised that, as New Zealand legislation requires, the clinic offers professional counselling to all women seeking an abortion and anyone showing signs of ambivalence about the procedure is referred to a counsellor to discuss their pregnancy options.
3. The Committee queried how the consent process worked, given the time critical nature of the VEMA procedure. The researcher advised the following process;
   * Once a woman identifies she is pregnant and contacts the clinic, she is booked in for an ultrasound appointment at the next available date.
   * On the day of appointment, the clinic performs a pregnancy test.
   * If the result is positive, the nurse discusses the decision (not in-depth as the law does not allow this) and advises what support is available (e.g. counsellor).
   * After the ultrasound a nurse discusses abortion options and offers VEMA (only if ultrasound shows no sign of pregnancy yet).
   * If the woman is ambivalent about the decision, she will not be enrolled in the study.
   * If the women consents to participating in the study she will have a medical examination by a doctor to ensure she is clear in her decision and healthy enough to undergo the procedure.
   * As it is time critical, the procedure is usually performed the same day if the woman consents and clears the medical assessment.
4. The Committee expressed concern about whether there is enough time for participants to consider the VEMA study and discuss with family given they are only made aware of the VEMA procedure when they arrive at the clinic. The researcher advised that the abortion process is lengthy and there is time during the day (in between the process steps above) for the woman to digest the information and decide.
5. The Committee asked if there is time for the woman to speak to a counsellor given the procedure happens in the same day. The researcher responded that the counsellors are usually booked up on the day which would be a problem. She advised that they could allocate a daily time slot in the counsellor’s diary for VEMA participants.
6. The Committee were in favour of that idea and recommended that the researcher consider additional options for ensuring that participants have as much lead in time as possible to ensure they have adequate support available to them and time to decide.
7. The Committed advised that undertaking Māori consultation is the applicant’s responsibility and not the participants as stated in answer to application question p3.4.3. Please amend this and provide evidence to the Committee.

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

1. Please provide more detail on Gynaecology Governance Group that is referenced on page 4.
2. Please ensure inclusion of the contact details for Māori Health support person.
3. Please add statement acknowledging the taonga status of Māori data under ‘Security and Storage of Your Information’ on page 6.
4. Please clarify the location of the ‘laboratory’ and turnaround time for results on page 3.
5. Please soften the language used in the paragraph beginning ‘'If an adverse event occurs” on page 4.
6. Please provide a lay summary to participants rather than the medical journal article (page 7).
7. Please clarify in the consent form that the participant can nominate a GP that is not their family doctor to provide test results to.
8. Please ensure the updated form includes the researcher’s (tracked) amendments as well as the Committee’s suggested edits (tracked) when resubmitting (e.g. remove mention of diaries).
9. Please carefully proofread the documentation for grammatical errors and spelling mistakes (e.g. “dairy” instead of “diary”).

Decision

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

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

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| **7** | **Ethics ref:** | **21/NTB/75** |
|  | Title: | MASTERPLAN |
|  | Principal Investigator: | Dr Iain Ward |
|  | Sponsor: | Australasian Gastro-Intestinal Trials Group |
|  | Clock Start Date: | 25 March 2021 |

Iain Ward 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 study is a prospective, international, randomised trial investigating the safety and activity of adding more highly focused and intense radiation treatment (known as stereotactic body radiotherapy or SBRT) to the standard of care chemotherapy regime for patients with high risk borderline or locally advanced Pancreatic cancer. 120 participants in total with six 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 noted the brief time they had to digest the evidence of peer review emailed to the HDEC secretariat today.
2. The Committee stated that peer reviews from international national health research council grant funders are not typically accepted. In this instance however, the Committee is comfortable to accept the Australian National Health Medical Research Council grant funding as evidence of peer review given the satisfactory supporting documentation provided.
3. The Committee asked for clarity on what chemotherapy regimen will be used in New Zealand as the protocol mentions two options, but the PSIF/CF has one. The Researcher confirmed that the treatment used will be mFOLFIRINOX as Paclitaxel is not funded in New Zealand.
4. The Committee noted that there are several quality of life questionnaires and asked what formats these will be available to participants in. The researcher advised that the intention is to use paper format but will extend to digital formats if the need arises.

Summary of outstanding ethical issues

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

1. The Committee requested confirmation from the researcher that the samples taken for future genetic research will only be identified by the participants study number only and no other identifiable details.
2. The Committee advised that as there are substantial changes required to the study documentation, these will need to come back to the HDEC for review.

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

1. Please translate the form from Australian to New Zealand specific (e.g. replace National Statement and HREC references).
2. Please adapt the data section to the ‘What will happen to my information?’ section from the [HDEC participant information template](https://ethics.health.govt.nz/system/files/documents/pages/participant-information-sheet-consent-form-template-sep20.doc) as it is better at distinguishing identifiable and coded data and who exactly has access to identifiable data.
3. Please remove the witness box on the consent form as this is not needed in New Zealand.
4. Please remove the withdraw consent form as that is not a requirement in New Zealand as it can be verbal.
5. Please consider making the PIS/CF less complex and the HDEC participant information sheet template will help with this. For example, the diagram in figure one is difficult to understand and could be simplified and provided later in the form.
6. Please add the sponsor address to the front-page headers.
7. Please amend the statement from “discuss these concerns with a kaumatua or whanau member” to “discuss with someone you trust”.
8. Please also indicate if there will be opportunity for karakia at the time of tissue disposal.
9. Please add a statement acknowledging taonga status of Māori data
10. Please ensure inclusion of Māori health/cultural support person details.
11. Please also contextualize the FUR PIS/CF to the New Zealand situation. E.g. that research may be conducted overseas and will not be approved by a New Zealand ethics committee or have any New Zealand representation.

Decision

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

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

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| **8** | **Ethics ref:** | **21/NTB/74** |
|  | Title: | VIR-2218-1006: Phase 2 study on VIR-2218 + VIR-3434 in Participants with Chronic Hepatitis B Virus Infection |
|  | Principal Investigator: | Professor Edward Gane |
|  | Sponsor: | Vir Biotechnology, Inc. |
|  | Clock Start Date: | 25 March 2021 |

Edward Gane, Courtney Rowse and Debbie 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 aims to find out how safe and well tolerated VIR-2218 combined with VIR-3434 is, and how this treatment works against HBV. Other goals of the study are to test whether VIR-2218 combined with VIR-3434 can reduce levels of HBV particles in the body and to measure the amount of VIR-2218 and VIR-3434 in the blood over time. A global study with 16 NZ participants.

Summary of resolved ethical issues

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

1. The Committee noted that the design study is complex involving a main study and two sub studies and asked how the informed process will work – for example do participants consent for the main study and one of the additional sub studies at the same time?
2. The researcher advised that yes, the randomised nature of the study design means they must enrol participants into both the main study and a sub-study together. He added that they intend to send the three participant information sheets to the potential participants prior to the screening visit. He added that at the visit they will discuss all three study designs with the participants so that the participant can make an informed choice as to which one of the two sub studies they want to participant in.
3. The Committee stated that the three study information sheets are very detailed and asked if they could be amalgamated or presented more simply across the cohorts to make the information more digestible for participants.
4. The researchers responded that the consents need to be separated because there are additional blood samples required in the sub study(s). The researchers, agreed, however that they could append information to make it easier for participants to refer to the relevant cohort study information once enrolled.
5. The Committee asked how researchers will allocate participants to the optional sub-studies. The researcher advised that participants can self-select as participant arrangement will not impact the rigour of the study.
6. The Committee queried why there is a payment offered for participation in the optional VIR-2218 PK sub-study but not the optional PBMC sub-study. The researcher advised that this is because the VIR-2218 PK sub-study requires additional visits to the clinic for blood sample collection.
7. The Committee noted that the application form states in question 3.3.1 that there will be no expense reimbursement for involvement in the studies which is contrary to the information being provided to participants. The researcher confirmed that this is an error and participants will be reimbursed as detailed in the participant information sheet and consent form (PIS/CF).
8. The Committee asked what arrangements there are for covering taxis and/or accommodation for participants who complete their clinic visits late at night. The researcher advised that taxis will be provided to local participants and accommodation provided to participants from outside the region.
9. The Committee noted that the application form states that there will be 16 participants in the study but the insurance certificate limits subject numbers to 10. The researcher advised that they will cap participant numbers to 10 across New Zealand.
10. The Committee noted that the Main PIS/CF states that “You should not drive or operate machinery until you know how the study treatment affects you” and asked if the researchers are anticipating post treatment effects. The researcher responded that they are fully aware of the safety profile of these drugs and do not consider this a concern.
11. The Committee queried why cannabis is excluded from the drugs of abuse listed on page 14 of the PIS/CF. The researcher responded that as there is no evidence of blood drug interactions with Hep B and cannabis, he sees no reason to include it.

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

1. Please add statement outlining the specific reporting requirements for HIV and hepatitis in New Zealand on page 5.
2. Please add the sponsor address to the front-page headers.
3. Please amend the statement “discuss these concerns with a kaumatua or whanau member” to “discuss with someone you trust".
4. Under the ‘What happens to my samples?’ section, please state whether there will be an opportunity for karakia at the time of tissue disposal.

Decision

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

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

## 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:** | 04 May 2021, 12:00 PM |
| **Meeting venue:** | ONLINE - Zoom Meeting |

1. **Review of Last Minutes**

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

The meeting closed at 4.01pm.