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| **Committee:** | Northern B Health and Disability Ethics Committee |
| **Meeting date:** | 02 March 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 February 2021 |
| 12:30pm | New applications (see over for details) |
| 12:30-12:55pm  12:55-1:20pm  1:20-1:45pm  1:45-2:10pm  2:10-2:30pm  2:30-2:55pm  2:55-3:20pm  3:20-3:45pm | i 21/NTB/40 (Tangihaere / Leesa)  ii 21/NTB/43 (Susan / Devonie)  iii 21/NTB/41 (Kate / Devonie)  iv 21/NTB/42 (Kate / Devonie)  [break]  21/NTB/44 (Susan / Steph)  21/NTB/45 (Tangihaere / Leesa)  21/NTB/46 (Kate / Steph) |
|  | Substantial amendments (see over for details) |
| 3:45-4:00pm | i NTY/08/06/055/AM20 (Full committee) |
| 4:00pm | General business:  Noting section |
| 4:05pm | 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 |
| Dr Devonie Waaka | Non-lay (intervention studies) | Co-opted | Co-opted | Present |
| Mrs Leesa Russell | Non-lay (intervention studies), Non-lay (observational studies) | 14/12/2015 | 14/12/2018 | Present |
| 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 | Apologies |
| 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 Dr Jane Wylie and Mr John Hancock.

The Chair noted that it would be necessary to co-opt members of other HDECs in accordance with the Standard Operating Procedures. Dr Devonie Waaka confirmed her eligibility, and was co-opted by the Chair as members of the Committee for the duration of the meeting.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

The Committee invited departing member Dr Nora Lynch to join the meeting for a farewell. The Committee acknowledged Dr Lynch’s expertise and thanked her for her contribution to the HDEC over the years.

## Confirmation of previous minutes

The minutes of the meeting of 02 February 2021 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **21/NTB/40** |
|  | Title: | ARISE FLUIDS |
|  | Principal Investigator: | A/Prof Peter Jones |
|  | Sponsor: | ANZIC Research Centre |
|  | Clock Start Date: | 18 February 2021 |

A/Prof Peter Jones 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. Sepsis is a life-threatening illness due to the body’s response to an infection damaging its own organs. Septic shock is a severe subset of sepsis with low blood pressure such that blood flow to tissues is inadequate. This requires emergency treatment to restore tissue blood flow and to control the infection.
2. The standard initial treatment is using IV fluids through a drip to restore blood pressure. Guidelines recommend 20-30 ml/kg (≈2-3 litres) in the first 3 hours. If this is insufficient, IV medication to raise the blood pressure is started. Many patients receive a combination of fluids and medications. Despite falling deaths from sepsis in the past two decades, evidence is emerging that excess IV fluids are associated with harm in sepsis. An alternative is to start medication earlier to reduce the amount of fluid administered. There is uncertainty about which is best for patients, and as a consequence practice varies between these approaches. As sepsis mortality has fallen, there is an increasing focus on quality of life among survivors. People who survive can have severe lifelong problems including persistent organ failure, amputated limbs, psychological injury and impaired function.
3. This trial will investigate if giving a smaller amount of IV fluid with early commencement of medication (“vasopressors”) to improve blood pressure leads to better patient outcomes than giving a larger amount of fluid before starting medication (“fluids”). Patients eligible for the trial will be randomly allocated to receive one of these treatment regimens. The main outcome we will measure is the number of days the patient has survived out of hospital at 90 days. This patient-centred measure was chosen in consultation with consumers and captures survival, illness severity and quality of life. The trial will recruit 1000 patients from emergency departments in hospitals throughout Australia and 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 requested justification for the Researcher’s case that the study is in the best interest of participants who cannot provide informed consent. The Researcher stated participants would receive more closely monitored care as part of the study. The Researcher explained there was often not dedicated one-on-one nursing in the emergency department resuscitation room and incoming patients can divert attention. The Researcher stated a dedicated research nurse would provide one-on-one nursing to participants. The Committee stated that as participants would receive additional care above the standard of care by being enrolled in the study it would accept the best interests argument.
2. The Committee queried how many patients arriving at the emergency department with septic shock would be able to consent for themselves and how it would be assessed. The Researcher stated the issue is even if a patient is potentially able to consent the treatment is life threatening and the informed consent process can take an hour. The Researcher explained with septic shock the patient will have impaired organ function by definition which may include cognitive impairment and a formal competency assessment would be time consuming. The Researcher stated they believe it would be difficult to do a proper informed consent process.
3. The Committee queried when the Researcher would ascertain the views from family members. The Researcher stated as soon as practically possible. The Researcher stated they are aware it is a stressful situation and family members will be upset so want to do it at the appropriate time.

Summary of outstanding ethical issues

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

1. The Committee queried the process for participants who die. The Researcher stated the data would need to be included to protect the scientific integrity of the study. The Committee suggested the Researcher contact Dr Colin McArthur as he has developed a tool to work through various scenarios.
2. The Committee requested an independent peer review and recommended the Researcher use the [scientific peer review template available on the HDEC website.](https://ethics.health.govt.nz/system/files/documents/pages/HDEC-Peer-Review-Template.docx)
3. Please insert a statement on page 29 of the protocol advising that the study will follow New Zealand ethical standards.
4. Please insert a statement into the protocol advising that ‘legally authorised person’ is not applicable in New Zealand.
5. The Committee recommended an amendment to the protocol to restrict the diary to participants able to provide informed consent and to contact the GP of those who can not to obtain their records.

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

Whānau PIS:

1. Please be clear on the length of time and type of access you are asking for with respect to medical records. When, what and for how long should be included in the PIS.
2. Please reword the statement following potentially coercive statement so it does not imply that someone will receive sub-standard care by not participating: “By participating in this research your relative/whanau/friend will have received the best available monitoring of their condition from the time they arrived at the Emergency Department, which means any change in their condition will have been detected and treated as soon as possible".
3. Please insert a statement into the alternatives section advising that if they choose not to continue there will be no impact on their relative’s care, or further treatment.
4. Please amend the section on future research on page 6 to be clear that only deidentified data will be used. Please state whether it is intended for future unspecified research or clarify parameters if it will be used for a known purpose.
5. On page 7 please insert a statement advising that all storage will comply with local requirements and be clear about how you will comply with the 2020 Privacy Act. This will require overseas storage to meet New Zealand privacy legislation (this can be assured via contract).
6. Please revise the right to withdrawal section to make it clearer. Clarify if the options are full withdrawal with all information from the study removed, withdrawal from the study but already collected data may be used etc.
7. Please provide full web address of clinical trial registry.
8. Please include a statement acknowledging the taonga status of Māori data.
9. Please ensure the inclusion of contact details for a Māori health / cultural support person in the PIS.

Consent Form:

1. Please remove ‘in my first language’ unless interpreters are offered and withdrawal consent in advance of withdrawal seems a little pre-emptive.
2. In the final statement please be clear who is agreeing to inform the participant - that responsibility should not fall on the whānau member, but the study team.
3. Please make it clear that study is slightly different depending on ward/ICU (duration).

PIS Participants post enrolment:

1. Please ensure the ‘What will happen to my information’ sections are aligned across both forms. The PIS participant one is more detailed.
2. Both forms need to be clearer about what is being asked at the phone calls (i.e. “we will complete two surveys about your general quality of life”).

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 the suggestions made by the Committee.

After receipt of the information requested by the Committee, a final decision on the application will be made by Miss Tangihaere MacFarlane and Mrs Leesa Russell.

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| **2** | **Ethics ref:** | **21/NTB/41** |
|  | Title: | PRM-151 STARSCAPE |
|  | Principal Investigator: | Prof Lutz Erwin Lothar Beckert |
|  | Sponsor: | Covance New Zealand Limited |
|  | Clock Start Date: | 18 February 2021 |

Prof Lutz Beckert was not 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 evaluate the efficacy, safety, and pharmacokinetics of PRM-151 compared with placebo in patients with idiopathic pulmonary fibrosis (IPF) during a 52-week period. At the end of this 52-week period, participants will be invited to enrol in an open-label extension (OLE) study to receive treatment with PRM-151.

Summary of outstanding ethical issues

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

1. Please clarify how Roche will link participant study data to other Roche study data for that participant, as stated in the PISCF. State what this will be used for and whether there are any limitations on linking. Clarify how this will be achieved, given Roche will be provided only with a participant ID number that is specific to the current study.
2. The data and tissue management plan is incomplete, please fill in the placeholders.
3. The data and tissue management plan states some samples will be listed with identifiers whereas the application says they will not. Furthermore, the data and tissue management plan says there is no biobank, but the application intends to bank samples for future use. Please clarify.
4. Please be aware that if a participant withdraws from the study (or fails screening) the onus is on the Researcher to ask if they are happy for samples to continue to be used for future research.
5. Please note that in New Zealand it is not permissible to terminate a study for commercial reasons.

Main PISCF

1. p5: State questionnaires will include questions about mental health.
2. p6. Give important self-screening eligibility criteria, in lay language.
3. p7. Take side effects out of box and use larger font. Very unclear why risks are discussed twice; please combine. Separate common risks from the anaphylaxis section and bullet point; give frequencies.
4. p9. Contraceptive requirements are listed for women and men in separate sections, but sperm donation is listed with female contraceptive requirements - please amend.
5. p9. Sperm donation is not permitted but there are seemingly no restrictions on egg donation despite the requirement for female participants to use contraception. Is this correct?
6. p13. Includes total FUR and genomic assays in mandatory tissue testing. Please remove this from the main PIS.
7. p14. Add 'identifiable information' as this is being collected during the study. Provide bullet points about who has access and why. Currently this is located in 'de-identified information', which is clearly incorrect. Significant repetition / confusion in this section should be addressed.
8. p15. Explain 'Your study data may be ..... linked to other data collected from you'. The DTMP states no data linking will be undertaken.
9. p15 / 17. Information about ownership rights is repeated.
10. Please include a statement acknowledging the taonga status of Māori data.
11. Please include a statement advising whether a karakia will be able to be performed at the time of tissue disposal.
12. Please include a statement advising participants that their GP will be asked to report any changes in physical or mental health to the study team.

FUR PISCF

1. Include risks of FUR / genomic research - tissue analysis / storage overseas - re-identification; potential for matching across DNA data banks (including familial matching with blood relatives).
2. Please delete the reference to a legally authorised representative from consent form as this is not consistent with New Zealand law.
3. Please include an appropriate cultural statement and Māori health contact.
4. Please include a statement advising whether a karakia will be able to be performed at the time of tissue disposal.

PREGNANCY PISCF

1. This is not to be submitted for review / approval unless a pregnancy is reported in a participant or partner. This can be submitted as an amendment if it occurs.

RELATED RECRUITMENT DOCUMENTS

1. Explain how these will be used; it will be tempting for participants not to refer to the PISCF given the multitude of other documents presented.
2. Informed consent flipchart: ensure frequencies of important risks are discussed with the patient. Include information on data and tissue management. Please ensure this does not replace a proper informed consent process with the PIS.

CAREGIVER LETTER

1. The timing of this letter is important and may not be sent out unless the participant has given consent for caregiver to be informed.

GP LETTER

1. Please include a list of drugs participants may not take while enrolled in the study.

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 the suggestions made by the Committee.

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

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| **3** | **Ethics ref:** | **21/NTB/42** |
|  | Title: | STARSCAPE OLE |
|  | Principal Investigator: | Prof Lutz Erwin Lothar Beckert |
|  | Sponsor: | Covance New Zealand Limited |
|  | Clock Start Date: | 18 February 2021 |

Prof Lutz Beckert was not 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 OLE study is being conducted to confirm the long-term safety, efficacy, and pharmacokinetics of PRM-151 in the treatment of eligible patients with IPF who have taken part in Study PRM-151-202 and received the open-label study drug (Cohort A) or completed the Phase III Study WA42293 (Cohort B) with PRM-151. Additionally, patients who have discontinued treatment from or have completed Study WA42293 and do not want to receive open-label PRM-151 in this study, will be invited to enroll in survival follow-up Cohort C.
2. Patients in Cohort C will not receive any treatment and will not undergo any safety or efficacy assessments during the study. Patients who discontinue treatment from Cohorts A and B will PRM-151F. Hoffmann-La Roche Ltd.
3. 15/Protocol WA42294, Version 2 automatically transition to Cohort C for long-term follow-up, unless they withdraw consent from 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. Please clarify how Roche will link participant study data to other Roche study data for that participant, as stated in the PISCF. State what this will be used for and whether there are any limitations on linking. Clarify how this will be achieved, given Roche will be provided only with a participant ID number that is specific to the current study.
2. The data and tissue management plan is incomplete, please fill in the placeholders.
3. The data and tissue management plan states some samples will be listed with identifiers whereas the application says they will not. Furthermore, the data and tissue management plan says there is no biobank, but the application intends to bank samples for future use. Please clarify.
4. Please be aware that if a participant withdraws from the study the onus is on the Researcher to ask if they are happy for samples to continue to be used for future research.
5. Please note that in New Zealand it is not permissible to terminate a study for commercial reasons.

Main PISCF

1. p5: State questionnaires will include questions about mental health.
2. p7. Take side effects out of box and use larger font. Very unclear why risks are discussed twice; please combine. Separate common risks from the anaphylaxis section and bullet point; give frequencies.
3. p9. Contraceptive requirements are listed for women and men in separate sections, but sperm donation is listed with female contraceptive requirements - please amend.
4. p9. Sperm donation is not permitted but there are seemingly no restrictions on egg donation despite the requirement for female participants to use contraception. Is this correct?
5. p13. Includes total FUR and genomic assays in mandatory tissue testing. Please remove this from the main PIS.
6. p14. Add 'identifiable information' as this is being collected during the study. Provide bullet points about who has access and why. Currently this is located in 'de-identified information', which is clearly incorrect. Significant repetition / confusion in this section should be addressed.
7. p15. Explain 'Your study data may be ..... linked to other data collected from you'. The DTMP states no data linking will be undertaken.
8. p15 / 17. Information about ownership rights is repeated.
9. Please include a statement acknowledging the taonga status of Māori data.
10. Please include a statement advising whether a karakia will be able to be performed at the time of tissue disposal.
11. Please include a statement advising participants that their GP will be asked to report any changes in physical or mental health to the study team.

FUR PISCF

1. Include risks of FUR / genomic research - tissue analysis / storage overseas - re-identification; potential for matching across DNA data banks (including familial matching with blood relatives).
2. Please delete the reference to a legally authorised representative from consent form as this is not consistent with New Zealand law.
3. Please include an appropriate cultural statement and Māori health contact.
4. Please include a statement advising whether a karakia will be able to be performed at the time of tissue disposal.

PREGNANCY PISCF

1. This is not to be submitted for review / approval unless a pregnancy is reported in a participant or partner. This can be submitted as an amendment if it occurs.

RELATED RECRUITMENT DOCUMENTS

1. Explain how these will be used; it will be tempting for participants not to refer to the PISCF given the multitude of other documents presented.
2. Informed consent flipchart: ensure frequencies of important risks are discussed with the patient. Include information on data and tissue management. Please ensure this does not replace a proper informed consent process with the PIS.

CAREGIVER LETTER

1. The timing of this letter is important and may not be sent out unless the participant has given consent for caregiver to be informed.

GP LETTER

1. Please include a list of drugs participants may not take while enrolled in the study.

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 the suggestions made by the Committee.

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

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| **4** | **Ethics ref:** | **21/NTB/43** |
|  | Title: | 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: | 18 February 2021 |

Dr David Worsley was not 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 52-week randomized, double masked, 2-arm, parallel study comparing the efficacy, safety and immunogenicity of SOK583A1 with Eylea® -an approved treatment - in 460 patients, age ≥50 with neovascular age related macular degeneration (nAMD). Both drugs contain the active ingredient aflibercept. Patients will be randomised to either drug on a 1:1 ratio and will receive a single intravitreal injection (IVT) at baseline, week 4, 8, 16,24,32,40 and 48 wks.
2. The primary endpoint is mean change from baseline in best corrected visual acuity (BCVA) at Week 8 and eye photographs. Patients will have efficacy and safety assessments prior to study treatment, including BCVA, blood and urine tests, physical exam, 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 what the patient is having.

Summary of outstanding ethical issues

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

GENERAL

1. The IP appears to be a biosimilar to Eylea, and as such the statement that it is 'the same active ingredient' cannot be made with any certainty. This is the first in human study of SOK583A1, which has not been mentioned anywhere in the application form or associated documents.

PARTICIPANT SAFETY

1. No sentinel dosing (generally required by HDECs for FIH, including biosimilarity studies). Clarify if dosing has commenced overseas, as this will nullify the issue.

DATA SAFETY MONITORING COMMITTEE

1. r.1.4 states an IDSMC will be utilised for the study, but r.1.5. provides only a description of routine CRA monitoring. There is no reference to any type of DSMC in the protocol. Confirm that an IDSMC is in place and provide the committee charter.

DATA MANAGEMENT

1. There is no clear data and tissue management plan for the study in the protocol or associated documents. The application has not answered the data management questions with any specificity; many of the responses seem to reference Australia (interstate, Federal and State laws etc), and it is unclear whether the Sponsor has processes in place to comply with New Zealand ethical and regulatory requirements. A DTMP is required. The Committee recommends adapting the [HDEC tissue and data management template.](https://ethics.health.govt.nz/system/files/documents/pages/hdec-data-tissue-management-template-oct2020.docx)

TISSUE MANAGEMENT

1. r.3. and subsequent responses mention 'genetic markers' several times, yet genomic analysis is not referenced in the protocol or any of the PISCFs. Clarify why this has been included and what genetic markers are intended to be analysed.
2. The response to r.3.8.1. suggests that all samples are stored long-term for non-specific future research. Please explain what is meant by 'The collection and analysis of these specimens will facilitate the rational design of new pharmaceutical agents and the development of diagnostic tests, which may allow for individualized drug therapy for subjects in the future.'
3. The response to r.4.1.1 is puzzling and discusses only the results of future research. Describe how incidental findings of potential clinical significance that arise during the study will be managed.

RECRUITMENT

1. Discuss whether patients will be given the opportunity to discuss study participation with a member of the research team not involved in their clinical care, to reduce the potential for feeling undue pressure to participate.

CONTINUATION OF INFORMED CONSENT

1. p.2.7 has not been answered appropriately. Discuss how participants will be made aware of important information about the study drug or study conduct that may impact their decision to continue taking part.

CULTURAL ISSUES

1. The cultural section has been answered very poorly. The importance of the disorder under study to Māori is not addressed.
2. The taking of tissue for research (including genetic research) and sending tissue overseas has not been addressed.
3. f.1.1. has been answered incorrectly. This study will not address health inequities.

SPONSOR INDEMNITY

1. The insurance certificate is not NZ-specific. Please amend accordingly.

MAIN PISCF

1. p1. A warning box is required, as this is the first time the biosimilar will be trialled in humans.
2. p2. states that 'it may be treated at the discretion of your Study Doctor with a standard treatment available in your country and not with the study treatment'. Does this mean the IP, or can Eylea also not be used? Please clarify.
3. p4. Amend 'Any treatments and medicines taken in your study and fellow eye in the past'; the participant has not yet entered the study.
4. p4. Explain 'demographics' 'respiratory rate' etc in lay terms
5. p8. Delete references to optional PK substudy from page 8.
6. p9. Para 3 states samples will be 'destroyed after analysis or by the end of the study'. Para 5 states 'The Sponsor may keep unused biological samples as part of the Coded Data .... for up to 15 years after the study ends and then destroy them', and that 'you can ask.... the Sponsor to stop using your samples at any time ....after the study.' Para 2 on page 10 states 'The samples will be destroyed once testing has been completed'. Reconcile these statements. Explain what samples will be used for after the study is completed.
7. p11. It is unclear why the risks table has been divided into 3 columns. Insert explanatory headings for each column if indicated, or merge into a single column to avoid confusion.
8. p19. Para 4 repeats information from p18; delete to avoid repetition.
9. p21. Section 15 repeats information from Section 11 (p20). Delete one set of text to avoid repetition.
10. p22. Correct the HDEC email address.

PK PISCF

1. Delete the optional tick box for continued use of information post-withdrawal; this is mandatory.

FUR PISCF

1. Make it clear that research could include genomic research. Explain genes, DNA etc in lay terms. State whether genomic research may include whole genome sequencing (and if yes, explain WGA in plain English).
2. Risks should include the risks of re-identification, particularly if future research includes genomic research. Make it clear that this risk may also impact on blood relatives. The risks of sending and storing tissue overseas should also be stated.
3. Remove the optional tickbox from the consent form

LETTER TO DOCTOR

1. Please make it clear that the referring physician should seek verbal consent from the potential participant prior to referring them to investigators.

CHART REVIEW CHECKLIST AND INCLUSION/EXCLUSION ASSESSMENT

1. The chart review checklist and inclusion/exclusion assessment card are out of scope for HDEC review and have not been assessed.

Decision

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

* Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
* Please supply details of the DSMC. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.25).*
* Please supply a data governance plan to ensure the safety and integrity of participant data

*National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15).*

* Please supply a tissue management plan *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 14.16).*

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| **5** | **Ethics ref:** | **21/NTB/44** |
|  | Title: | TC-01-002: A study comparing Actemra®, RoActemra® and DRL\_Tocilizumab, in healthy adults. |
|  | Principal Investigator: | Dr Christian Schwabe |
|  | Sponsor: | Syneos Health |
|  | Clock Start Date: | 18 February 2021 |

Dr Christian Schwabe 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. Actemra® and RoActemra® (tocilizumab) are currently approved for the treatment of rheumatoid arthritis and other inflammatory disorders.
2. Dr Reddy's Laboratories has developed its own preparation of tocilizumab, called DRL\_Tocilizumab (DRL\_TC). This study aims to show that DRL\_TC is very similar to tocilizumab approved in Europe (RoActemra®) and the USA (Actemra®), in terms of:

- Levels of drug in the blood over time.

- Safety and side effects.

- Effects on inflammation markers and lipids (fats) in the blood.

- Production of antibodies (immune system proteins) against the drug.

1. Approximately 300 healthy men and women will be enrolled in the study.
2. Participants will receive two 162 mg doses of tocilizumab during the study, with a gap of 6 weeks between doses.
3. Participants will be randomly assigned to one of the following 6 treatment arms:

- DRL\_TC followed by Actemra®

- Actemra® followed by DRL\_TC

- DRL\_TC followed by RoActemra®

- RoActemra® followed by DRL\_TC

- Actemra® followed by RoActemra®

- RoActemra® followed by Actemra®.

1. Each dose will be administered as an injection under the skin in the upper arm (a subcutaneous or 'SC' dose).
2. A sentinel dosing approach will be used, where 3 participants will be dosed and monitored for at least 96 hours prior to further enrollment. Sentinel participants will be randomised 1:1:1 to DRL\_TC, Actemra®, and RoActemra®.
3. Blood samples to measure study drug levels, markers and antibody response will be collected at specific time points; safety will be monitored; and any changes in health will be recorded.
4. The results will be used to inform further development of DRL\_TC.

Summary of outstanding ethical issues

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

1. The Committee queried how the Covid-19 vaccine rollout may affect participation in the study. The Researcher stated they believe the overlap would be minimal but would clarify with the sponsor.

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

1. Please ensure Māori health support contact details are inserted into each site-specific PIS.

Decision

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

* Please clarify how the Covid-19 vaccine rollout will be managed.
* Please update the Participant Information Sheet and Consent Form, taking into account the suggestion made by the Committee.

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| **6** | **Ethics ref:** | **21/NTB/45** |
|  | Title: | Phase I GDC-6036 in patients with solid tumors |
|  | Principal Investigator: | Dr Sanjeev Deva |
|  | Sponsor: | PPD on behalf of Genentech, Inc |
|  | Clock Start Date: | 18 February 2021 |

Dr Sanjeev Deva 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. GDC-6036 is an oral, covalent, anti-cancer therapeutic agent that selectively inhibits KRAS G12C, but not other mutations in KRAS, the wild-type form of KRAS, or other members of the RAS family. Nonclinical studies demonstrate that treatment of KRAS G12C positive cancer cell lines or tumour xenograft models with GDC-6036 results in decreased KRAS pathway signalling, suppression of proliferation, and induction of apoptosis.
2. The results of nonclinical toxicology studies completed to date provide a robust characterization of the toxicity profile of GDC-6036 and support the administration of GDC-6036 in a first-in-human Phase I trial in patients with cancer.
3. This is a first-in-human Phase Ia/Ib, open-label, multicentre dose-escalation and dose expansion study designed to evaluate the safety, pharmacokinetics, and preliminary activity of GDC-6036 as a single agent and in combination with other anti-cancer therapies in patients with advanced or metastatic solid tumours that harbour the KRAS G12C mutation. The combination therapies in this study are atezolizumab (Arm B), cetuximab (Arm C), bevacizumab (Arm D), and erlotinib (Arm E) in NSCLC, CRC, and solid tumours. The study is designed with the intention to include new, additional treatment arms during study conduct to explore combinations of GDC-6036 with other anticancer therapies based on emerging nonclinical and clinical data with GDC-6036, other KRAS G12C inhibitors, or evolving standard-of-care treatment. Anticipated future combinations with GDC-6036 may include RTK/RAS/MAPK pathway-targeting therapies, agents that target compensatory pathways that may mediate intrinsic or acquired resistance to treatment, immunotherapies, agents that modulate the tumour microenvironment, and standard-of-care agents to further explore safety, pharmacokinetics, and preliminary activity.

-Arm B (GDC-6036 and Atezolizumab)

-Arm C (GDC-6036 and Cetuximab)

-Arm D (GDC-6036 and Bevacizumab)

-Arm E (GDC-6036 and Erlotinib)

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 the response to r.1.6. in the application form and advised that studies may not be terminated for commercial reasons in New Zealand.
2. The Committee requested the Researcher supply a tissue and data management plan and recommended adapting the [HDEC tissue and data management template.](https://ethics.health.govt.nz/system/files/documents/pages/hdec-data-tissue-management-template-oct2020.docx) Please ensure the tissue and data management plan contains a Māori tissue and data sovereignty statement.
3. The Committee noted the MPS certificate expires shortly, please supply a new one.

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

Mutation Testing / Screening Consent

1. Please remove the future unspecified research clause and insert information explaining that if participants test negative their data will not be used. If participants test positive they can consent to future use on the FUR form.
2. Please remove information about the cost of the study drug from the mutation testing / screening PIS.

Main Study PIS

1. Please ensure the ACC wording in the [HDEC template](https://ethics.health.govt.nz/system/files/documents/pages/participant-information-sheet-consent-form-template-sep20.doc) is used and remove the additional information inserted before the HDEC paragraph.
2. Please insert a statement in the screening PIS advising that medical information will only be used for screening purposes and will not be used for other purposes in the future.
3. Please give more certainty around time commitments required for the study and duration of visits as one to eight hours is a wide variation. Please clarify if all appointments will be potentially eight hours or if different appointments will have different time lengths.
4. Please clarify exactly what non-FUR samples for the study will be used for (e.g. X is tested for or used for purpose Y) instead of a list of possible uses. Scientific explanation of advanced testing is not necessary and a simple statement specifying the use is sufficient.
5. Please insert a statement advising that parking and petrol costs can be reimbursed and clarify if there is an upper limit.
6. Please include a limit on how long participant health data will be retained (e.g. 20 years after the study concludes).
7. Please include the relevant information from the data management plan into the PIS so participants understand the privacy protections and uses of their information.
8. Please ensure the inclusion of a Māori health / cultural support person in the contact section.

Arm B PIS:

1. Please specify which countries samples may be sent to.

Arm C PIS:

1. Please undertake a general revision to correct the typos and formatting errors in this PIS.

Optional tissue photography:

1. Please make it clear how the clinical photography will be deidentified with regard to distinctive features, tattoos etc.

FUR PIS

1. Please remove the statement on removing identifiers from samples on withdrawing as withdrawing from the study should mean consent to use samples is withdrawn also.
2. Please clarify what happens or how long tissue will be stored for if participants do not tick the box to retain samples for 15 years.
3. Please add the study sponsor’s address to all information sheets.
4. Please insert information advising whether a karakia will be possible at the time of tissue disposal.

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 the suggestions made by the Committee.

After receipt of the information requested by the Committee, a final decision on the application will be made by Miss Tangihaere MacFarlane and Mrs Leesa Russell.

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| **7** | **Ethics ref:** | **21/NTB/46** |
|  | Title: | A Study to Assess the Efficacy and Safety of Vatiquinone for the Treatment of Friedreich Ataxia(MOVE-FA) |
|  | Principal Investigator: | A/Prof Richard Roxburgh |
|  | Sponsor: | Pharmaceutical Solutions Ltd |
|  | Clock Start Date: | 18 February 2021 |

A/Prof Richard Roxburgh and sponsor representatives Miriam Rodriegues, Kay Yeoman, Traci Schilling, Gareth Corbett, Pavels Anetko, Àine Tyson-Flynn and Gina Giannantoni-Ibelli 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 is a Phase 2b/3 study with an open-label extension to assess the efficacy and safety of Vatiquinone for the treatment of Friedreich Ataxia (MOVE-FA). This study will be a stratified, randomised, parallel-arm, double-blind, placebo-controlled trial.
2. The main objective of the study is to evaluate the efficacy, using the modified Friedreich Ataxia Rating Scale [mFARS]) and safety of vatiquinone in subjects with Friedreich ataxia (FA). For full objectives, refer to protocol pg. 25-26.
3. Subjects will be randomised 1:1 to receive either vatiquinone or placebo. The study duration will be approximately 106 weeks; 6 weeks screening, 72 weeks of randomised, double-blind, placebo-controlled treatment, 24 weeks of open-label extension treatment and approximately 4 weeks post-treatment follow-up.
4. Assuming a dropout rate of 10%, a total of 106 subjects between 7 and 21 years of age will be randomised. The primary efficacy analysis will be based on change from baseline in mFARS score of subjects between 7 and 21 years old. In order to explore the treatment efficacy and safety, up to an additional 20 subjects >21 years of age will be randomised for a total of 126 subjects.
5. The study will be conducted in approximately thirteen sites globally and there will be one site 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 long timeframe some participants would be on a blinded placebo for and queried if an interim analysis was planned that could shorten this. The Researcher stated it was not planned as disease progression is slow so it would take the full duration to detect an effect from the drug.
2. The Committee queried the purpose of the study brochure. The Researcher explained it is there for use if necessary, for supplementary information or as a basic introduction. The Researcher confirmed it would never be used instead of the PIS.

Summary of outstanding ethical issues

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

1. Please outline a safety plan in the protocol to manage a participant who indicates distress or suicidal ideation in the quality of life questionnaire. Please include details of what the follow-up will be in the PIS.
2. Please revise the exclusion criteria to exclude potential participants with a sesame allergy and include this in the list of stopping rules.

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

1. Please insert a statement into the PIS advising participants to let a research staff member know if they feel fatigued during the visits.
2. Please ensure there is a local contact number of all advertisements and remove the American phone number. Please add the HDEC reference for the study to all advertisements.
3. Please remove any references to a ‘legally authorised representative’ on the consent form as this is not applicable in New Zealand.
4. Please add information that the travel vendor will receive some identifying information in the relevant section on page 14 of the PIS and parent/guardian PIS.
5. Please make the assent form more child friendly by adding a tickbox.
6. Please include a statement advising whether a karakia will be available at time of tissue disposal on page 8 of the PIS.
7. Please revise the statement to discuss with kaumatua or whānau to simply state someone you trust.
8. Please revise the 12-15-year-old sheet to be less reserved about ‘things’ leading to pregnancy and simply name them.
9. Please remove the statement on the consent form related to blood samples and future unspecified research.
10. Please include a statement advising that the treatment contains pork product in case a potential participant has dietary or religious restrictions.

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 the suggestions made by the Committee.

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

## Substantial amendments

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| **1** | **Ethics ref:** | **NTY/08/06/055/AM20** |
|  | Title: | Growing Up in New Zealand |
|  | Principal Investigator: | Prof Boyd Swinburn |
|  | Sponsor: |  |
|  | Clock Start Date: | 25 February 2021 |

Prof Boyd Swinburn 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.

Mrs Leesa Russell declared a conflict of interest and would relinquish voting rights and not participate in the discussion.

Summary of study

1. This amendment pertains to the upcoming 12 Year data collection wave (to be trialled with the Leading Light group), along with a proposal for consulting with the LL group in regards linking all previously obtained study data, and that of the next wave, to the IDI. The original Coordinating Investigator has recently been replaced. The committee noted supplementary correspondence received on behalf of some named investigators who wished to express their disquiet about aspects of the study moving forward which they did not feel had been addressed adequately by internal processes to date. The committee had a robust and lengthy discussion.

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 seeks reassurance of how the current study steering group will resolve differences between any expectations of study funders and the kaupapa of the study from inception and through the regular retention activities, as this could be perceived as a conflict of interest.
2. Please submit the strategy for communicating to and reassuring participants in regards significant study changes (i.e. the change of CI, changes to data sovereignty).
3. The Committee noted that the final decision with regards the use of linked data in the IDI will rest with Stats NZ, and that this was a departure from the reassurances of sovereignty by the University of Auckland given to participants over time. Please submit documentation with terms of an agreement for how the data advisory group will work with Statistics New Zealand on using linked data. The HDEC requested reassurance that Statistics New Zealand will defer to the advisory committee’s opinion on whether it will use linked data in particular circumstances.
4. The Committee stated its preference for the data linking is to wait additional years until participants are 16 and can consent for themselves. The Researchers explained it takes three years to prepare the data for linkage so this would require waiting until participants are 16 and then a further three years to link the data. The Committee queried if the plan is to assent the participants when they are 12 to do the linking now. The Researchers stated they would ask the mother for consent about whether her and her child’s data would go into the IDI. The Researchers stated most of the data has been collected from the mother and even if participants were 16 her consent to link the data would be required. The Researchers stated they could not guarantee a data collection would happen when participants were 16 as study funding for that long has not been secured. The Committee requested the Researchers submit an amendment after consultation with the Leading Lght group with their feedback (and to complete the necessary consultation with other stakeholders such as the Asian community) before approaching the 12-year olds for assent and their mothers for consent for linking.
5. The Committee queried whether the communication contained adequate information about the IDI and what data it contains and if it is a fair representation of benefits and risks. The Researcher stated additional information was available and could be added.
6. The Committee queried whether data may be shared with overseas researchers. The Researchers stated at the moment overseas researchers can access the GUNZ data through the University of Auckland but would have to physically be in New Zealand to do so. The Committee requested information explaining this be added to the PIS.
7. The Committee recommended adapting the data section from the [HDEC PISCF template](https://ethics.health.govt.nz/system/files/documents/pages/participant-information-sheet-consent-form-template-sep20.doc) to ensure it contains all necessary information about data protection, any potential future uses etc.
8. Please include a caveat that if the dataset is used by overseas researchers in the future it would likely be done so without any input from New Zealanders.
9. The Committee requested the Researchers supply a data management plan that complies with [Chapter 12 of the National Ethical Standards for Health and Disability Research and Quality Improvement](https://neac.health.govt.nz/national-ethical-standards-health-and-disability-research-and-quality-improvement/part-two/12-health).
10. The Committee queried whether saliva samples previously collected for the study were in storage. The Researcher confirmed samples were stored by the University of Auckland. The Committee requested the Researchers supply a stringent tissue governance and management plan for this tissue repository that complies with [Chapter 14 of the National Ethical Standards for Health and Disability Research and Quality Improvement](https://neac.health.govt.nz/national-ethical-standards-health-and-disability-research-and-quality-improvement/part-two/14-human).
11. The Committee recommended adapting the [HDEC data and tissue management template.](https://ethics.health.govt.nz/system/files/documents/pages/hdec-data-tissue-management-template-oct2020.docx)
12. The Committee queried why new saliva samples would be taken if these had already been collected. The Researchers stated it would be to analyse any environmental effects on gene expression. The Committee requested a lay-friendly explanation of epigenetics so participants understand exactly what it will be used for. The Committee stated that future unspecified genetic research for minors is generally not approved by HDECs so the Researchers would need to be very specific on what testing they wish to do on the saliva samples, and remove suggestions of unspecified future genetic research. The Committee stated this would apply to the current samples in storage as well as future samples taken.
13. The Committee noted the process of going through the Board and Principal for teacher survey is acceptable, but the children were not being informed that their teacher would be answering questions about them. The Researchers stated they would include this in the assent form. The Committee requested the explanation include more specific information about the type of questions that will be asked (e.g. how the participant gets along with other children, their behaviour -especially problematic, how well they perform in school, parental engagement with the teacher etc). The Committee recommended this be an optional component of the study.
14. The Committee requested more information be given to parents about the teacher survey as the explanation to the mother does not currently convey the nature of the personal questions that will be asked.
15. The Committee requested information about the recorded conversation with the mother about ‘a problem area’ be added to the assent form.

**Provisionally approved:**

* **The Leading Light group to be approached on data linking only, and to take part in the pilot of the next data collection wave upon receipt of the data and tissue management plan and updated information sheets and consent forms.**

**To submit as a new amendment:**

* **Please submit the report on the consultation if the main cohort is to be approached for linking to the IDI**
* **Data sharing agreement with Stats New Zealand.**
* **Amended protocol with tighter restrictions on intended use of tissue.**
* **Updated information sheets and consent forms.**

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 the suggestions made by the Committee.

After receipt of the information requested by the Committee, a final decision on the application will be made by the Northern B Health and Disability Ethics Committee.

## 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:** | 06 April 2021, 12:00 PM |
| **Meeting venue:** | ONLINE - Zoom Meeting |

The following members tendered apologies for this meeting.

* Mrs Leesa Russell

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 4:30 pm.