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| **Committee:** | Northern B Health and Disability Ethics Committee |
| **Meeting date:** | 06 July 2021 |
| **Meeting details:** | <https://mohnz.zoom.us/j/9738756003>  Meeting ID: 973 875 6003 |

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| **Time** | **Item of business** |
| 12.00pm | Welcome |
| 12.15pm | Confirmation of minutes of meeting of 01 June 2021 |
| 12.30pm | New applications |
| 12.30-12.55pm  12.55-1.20pm  1.20-1.45pm  1.45-2.00pm  2.00-2.25pm  2.25-2.50pm  2.50-3.15pm  3.15-3.30pm  3.30-3.55pm  3.55-4.20pm  4.20-4.45pm | 21/NTB/150 Kate/Stephanie  21/NTB/165 John/Leesa  21/NTB/157 Susan/Stephanie  Break (15 minutes)  21/NTB/158 Kate/Leesa  21/NTB/159 John/Stephanie  21/NTB/161 Susan/Leesa  Break (15 minutes)  21/NTB/162 Kate/Stephanie  21/NTB/163 John/Leesa  21/NTB/156 Susan/Stephanie |
| 4.45pm | 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 |  |
| 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 | Present |  |
| Mr John Hancock | Lay (the law) | 14/12/2015 | 14/12/2018 | Present |  |
| Ms Susan Sherrard | Lay (consumer/community perspectives) | 19/03/2019 | 19/03/2022 | Present |  |

## Welcome

The Chair opened the meeting at 12pm and welcomed Committee members.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

## Confirmation of previous minutes

The minutes of the meeting of 01 June 2021 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **21/NTB/150** |  |
|  | Title: | Neonate Stoma Refeeding Device Study |  |
|  | Principal Investigator: | Mr Andre Modesto |  |
|  | Sponsor: | CureKids NZ |  |
|  | Clock Start Date: | 24 June 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 researchers are as follows.

1. The Committee acknowledged the effort the researchers made to address the issues set out in the HDEC’s decline letter and resubmit a quality application. There are, however, a few inconsistencies remaining that need resolving.
2. The Committee noted the peer reviewer’s concerns about low recruitment numbers and queried if the researchers planned to address this feedback (e.g. if there are plans to invite more sites to participate). The researchers confirmed their intention to start small with the Auckland site initially before being joined by the Christchurch and Wellington sites. The researchers added that the Australasian paediatric surgical network has shown strong interest and the Australian centres may begin their own trials following completion of the New Zealand centres.
3. The Committee observed that while the Investigator’s Brochure submitted is not best practice, they acknowledge that there is some device information included and that once the trial is complete, there will be more product information available to inform the Investigator’s Brochure.
4. The Committee noted the researchers’ confirmation that parents will not be expected to maintain the device on their own as the device will only be used under supervision by the trained study staff.

Summary of outstanding ethical issues

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

1. The Committee recommended, for safety purposes, a sentinel/staged entry approach, over a reasonable period (e.g. two to four weeks), given this is a first-in-human study that involves medically vulnerable infants. A staged approach where one or two participants complete the protocol before the next tranche are enrolled allows time to train staff, to monitor for adverse events, and to ensure the trial is running as expected overall. The researchers were comfortable with this approach and confirmed they will adjust their protocol accordingly to allow them to monitor one case at a time and report safety findings to the Auckland committee’s high-risk registry for review.
2. The Committee advised that there are inconsistent statements about future use of data and a use of a databank in the Data and Tissue Management Plan (DTMP) and Participant Information Sheet and Consent Form (PIS/CF) and asked for clarity. The researchers advised that, at this stage, there are no plans to establish a long-term database and will confine the use of data to this study only.
3. The Committee stated that it is reasonable to want to use the data collected from this feasibility study for future use, it just needs to be clear to participants what the data practices are going to be. The Committee requested that the researchers review the DTMP and participant facing documentation to ensure that their plans around future use of data are described accurately, consistently, and clearly.
4. The Committee requested that more detail is added to section 10 of the DTMP, explaining how personal information from standard of care samples will be managed. For example, how they will be de-identified for use in this study. Please also remove reference to sections 7.1 and 7.2 as these are not relevant.
5. The Committee requested that a table is added to the protocol, for clarity purposes, detailing the study visits, procedures, screening and timeframes (i.e. which procedure will be undertaken at which visit, how many visits, when, how long between screening and enrolment and enrolment to procedure/use, and follow ups, etc.) The Committee added that this is especially important when rolling out to multiple sites to ensure the protocol implementation is consistent.
6. The Committee requested the protocol clearly states if the trial design includes an open label crossover as this is unclear in the current document.
7. The Committee advised that information about the pictures and videos of stoma are missing from the protocol and DTMP and requested this is added.
8. The Committee advised that the protocol does not include what training will be provided to staff (and by whom) to avoid user error with the device.

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

*Nurse PIS/CF*

1. Please refocus the Nurse PIS/CF to be specific to that audience i.e. advising nurses on what their involvement in the study requires and revising the language used throughout the document (e.g. ‘your child’).
2. Please remove the declaration by the parent/guardian section.

*Main PIS/CF*

1. Please add the sponsor on page 1.
2. Please replace the compensation statement in the ‘What if something goes wrong?’ section with the approved HDEC statement in the [PIS/CF Template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc) on the HDEC website.
3. Please identify which co-investigators have a dual role with the sponsor as well as an academic role.
4. Please change the language from ‘your’ to ‘your child’s’ (e.g. ‘your hospital records’) or add a clarifying sentence to the beginning of the form defining what is meant by the term ‘your’.
5. Please remove reference to submitting information to a databank if this is no longer happening.
6. Please remove mention of returning results of screening and safety tests as the blood tests are routine and results will be returned to participants regardless.
7. Please moderate the offer of benefits as these cannot be assured in a first-in-human trial.
8. Please include more information about the photos in the data section to reassure participants – i.e. that these will be of an unidentifiable region of the body.
9. Please add more detail on procedures and timeframes so that parents have a good understanding of what is happening and when (i.e. use the table from the protocol once developed).
10. Please amend the Future Research section if you are not going to use data beyond this study (please note for future information sheets, that future use of data does not have to be optional and can be mandatory).
11. There is reference to data linking in the PIS/CF but it is unclear in all documentation what kind of data linking is being undertaken. Please remove the refence to data linking or couch it more broadly for future use (e.g. it will only be used with regards to this device).
12. Please add the funder, Cure Kids.

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 Stephanie Pollard and Mrs Leesa Russell.

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| **2** | **Ethics ref:** | **21/NTB/165** |  |
|  | Title: | TRANSFORM-1: M16-191 A Phase 3 Study of Navitoclax Plus Ruxolitinib Versus Ruxolitinib in Subjects with Myelofibrosis |  |
|  | Principal Investigator: | Dr James Liang |  |
|  | Sponsor: | AbbVie |  |
|  | Clock Start Date: | 24 June 2021 |  |

Dr James Liang 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 purpose of this study is to evaluate the effect of navitoclax in combination with ruxolitinib on splenomegaly response when compared to ruxolitinib in patients with myelofibrosis. There are two arms in this study. Participants will be randomised 1:1 ratio to either Arm A which is the experimental group receiving navitoclax and ruxolitinib or Arm B which is the control group receiving placebo to match navitoclax and ruxolitinib. 230 patients globally across 190 centres (small numbers at each), 10 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 acknowledged the good quality application and advised that the main issues involve tightening up detail in the study documentation.
2. The Committee informed the researcher that in New Zealand a therapeutic study cannot be stopped simply for reasons of commercial interest. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.37).*
3. The Committee noted that the answer to application question p.4.2 does not mention a karakia, however other documentation does. Please bear this in mind for future applications.
4. The Committee noted that an application is being submitted to the Standing Committee on Therapeutic Trials (SCOTT) in parallel to this study and will be provided to HDECs, as a peer review, once available.

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 Participant Information Sheet and Consent Form (PIS/CF) references collecting ‘survival’ data for up to 8 years after the study concludes but does not explain how this may occur or what the family member’s role is. While it is a pragmatic decision to include calls to family members if participants become too ill to respond to the follow up questions, this possibility needs to be carefully and clearly explained to participants and consent obtained up front.
2. The Committee suggested that consideration should also be given to how the follow up process will practically work (e.g. establishing ongoing contact with family members or nurses at residential care homes for example). The Committee recommended that the researcher develop a one-page information sheet for family members explaining this (excluding consent).
3. The Committee stated that it is unclear in the PIS/CF if biomarkers are an optional or mandatory component of the study. As it can be difficult for participants to digest a lot of information and delineate between mandatory and optional elements of a study, the Committee suggested separating the optional (bio-marker) information out into the additional consent form and only reference it in the Main PIS/CF (e.g. ‘we might look at bio-markers in this study to….if you’re interested then…’).
4. The Committee advised that the application and supporting documentation is inconsistent on whether there is future unspecific research (FUR). For example, the application form indicates that there will be FUR but the separate consent is missing. The Committee further clarified that FUR is not the same as the biomarker sub-study which is specified use and therefore they need to be treated separately. Please confirm whether or not FUR is required and update the protocol, Data and Tissue Management Plan (DTMP), and PIS/CFs accordingly.
5. The Committee requested that information about data linking is detailed in the DTMP and PIS/CF or taken out if it is not relevant.
6. The Committee noted the Pregnant Partner PIS/CF data release and requested that a justification is provided to HDECs for why information on past pregnancies is required for this research (rather than just current information).
7. The Committee suggested that the researcher reconsider the answer on reduction in inequity (application questions f.1.1 and f.2.1) as cancer is a significant cause of amenable mortality in Māori in New Zealand and is relevant for this study (i.e. 20 percent more likely to get cancer and twice as likely to die from cancer).
8. The Committee stated that providing a transparency statement (i.e. link to the Counties Manukau District Health Board website) in section 3 of the DTMP is not the correct policy for data governance in a study such as this. Please provide information that answers the question of ‘how will the data be governed and by who?’ Please also note that the website link currently provided is broken.
9. The Committee stated that section 4 of the DTMP refers to mandatory secondary uses of data but there are no optional secondary data uses described in the PIS/CF. Please either include them in the PIS/CF or remove them from the DTMP.
10. The Committee advised that information on privacy breaches for children under 16 years old should inform the parent/guardian, not the child, and requested that this is revised in the DTMP.
11. The Committee stated that if tissue samples are being shared with third party researchers (e.g. companies working with the sponsor), this needs to be included in the DTMP and the PIS/CFs.
12. The Committee advised that any updates to tikanga from Māori consultation that results in changes to the DTMP will need to be submitted to HDECs for review via the post approval (amendment) pathway.
13. The Committee requested that the researcher identify the current United States labs in the DTMP, even if they are subject to change (and which will require an amendment submitted to HDECs through the post approval pathway).
14. The Committee requested clarity on the purpose of the patient pamphlet as it appears to be a consent document, however, the PIS/CFs should be the only documents used for consenting. The Committee suggested considering repurposing the pamphlet as the family members information sheet.
15. The Committee requested that the doctor-patient letter explains what an investigational product is (i.e. a drug in development, the effects of which are not yet confirmed by scientific and clinical research).

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

1. Please review all patient facing documentation to ensure participants have a clear understanding of exactly what will happen and when, what will be collected/used, and how. The current wording of the documents is too broad and needs to be more specific.
2. Please also review medical language for lay readability and use simpler language that your everyday person could understand (e.g. the terms investigational product, treatment arms, placebo, and pre-clinical are all used repeatedly without, or prior to, explanation).
3. Please review paragraphs for long sentences and shorten them (e.g. the last paragraph on page 2).
4. Please simplify the reasons for discontinuing the trial as they are currently too complex.
5. Please clarify the following reimbursement statements, ‘up to a reasonable amount’ and ‘paid periodically’. Please be transparent about what the participant will receive and define the criteria for reimbursement in lay language (e.g. if parking will be paid, if taxi chits will be provided, if petrol vouchers will be provided, if there will be a koha offered, what limits there are (e.g. ‘petrol vouchers will be offered up to the limit of $...’)
6. Please clarify what happens after 24-week withdrawal as it is unclear if this is voluntary withdrawal or if participants are removed from the study for a particular reason.
7. Please define the exact nature of the 8-year data collection referenced on page 3, such as where the data is being sent (e.g. name and location of public databases and who has access to the data, etc.)
8. Please explain that family members may need to be contacted to collect the follow up (‘survival’) data in the body of the information sheet and add a clause to the consent form (as per the issue detailed above by the Committee).
9. Please include information about data linking or remove it if it is not relevant (as per Committee’s point above).
10. Please amend the wording throughout the document to make it clear whether or not the biomarkers are ‘required’ or optional. If optional, please create a separate biomarkers PIS/CF (as per the Committee’s point above).
11. Please specify what local and central labs are being used (i.e. add name and address).
12. Please clearly explain that participants may not be able to receive the COVID-19 vaccine while enrolled in this trial and that the study investigator will decide if this is the case. If receiving this vaccine is an exclusion/withdrawal criterion, please also state this.
13. Please be more explicit on the reason for including the following statement in the risk section on page 7, ‘Ruxolitinib which is a non-AbbVie drug is being used in combination with navitoclax’. For example, state the actual risk is that the drugs are manufactured and managed by two different companies which do not share information about formulation, etc. and what the result of that is.
14. In addition, please list all risks in a table in a separate section, from most serious risk to least serious, irrespective of how they occur (e.g. PML, platelet issues, Hepatitis B reoccurrence, etc.) and link each to the drug in the table. This table should also outline symptoms and say what participants should do if they notice symptoms.
15. Please move reference to biological specimens from page 12 to elsewhere in the document as these are not considered personal health information.
16. Please review the [HDEC’s PIS/CF template](https://ethics.health.govt.nz/system/files/documents/pages/participant-information-sheet-consent-form-template-sep20.doc) 'What happens to my information section?' and incorporate relevant components into the PIS/CF such as secondary use of data.
17. Please detail exactly what personal health information will be collected, rather than state that personal information ‘may be’ collected.
18. Please specify the exact duration that data will be held if participants do not revoke consent (page 13). This should not be indefinite.
19. Likewise, please replace 'storage period' with a specific storage time.
20. Please define the local laboratory for the test samples (i.e. either ‘in the hospital where you receive your treatment’ or include the name and address).
21. Please include information on whether or not karakia can be performed in the body of the information sheet (e.g. specify if it is at blood draw or at disposal and if it will not be done in overseas labs, etc).
22. Please include egg donation as an exclusion for participants due to the potential pregnancy harms.
23. Please include references to the patient identification cards and other cards given how these will be used.
24. Please include what the scope of ‘people/companies working with Abbvie' would be (as per the Committee’s point above).
25. Please make it clear whether or not data and/or tissue samples will continue to be used if the participants withdraw (as per section 13 of DTMP). If you would prefer to continue to use the participant data after withdrawing, please state this.

*Optional Biomarkers*

1. Please add addresses for the laboratories as stating country alone is not adequate as per the point stated earlier.
2. Please include information on whether or not karakia can be performed in the body of the information sheet (e.g. specify if it is at blood draw or at disposal and if it will not be done in labs overseas, etc).
3. Please specify the scope of ‘people/companies working with Abbvie' (e.g. clarify what will be sent and when).
4. Please distinguish between biomarkers and FUR (as per the Committee’s earlier point) and include a separate form for FUR, if applicable, using the [FUR PIS/CF template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/future-unspecified-use-tissue-piscf-template.doc) available on the HDEC website.

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 Leesa Russell and Mr John Hancock.

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| **3** | **Ethics ref:** | **21/NTB/157** |  |
|  | Title: | NIRTURE Trial |  |
|  | Principal Investigator: | Dr Maria Saito Benz |  |
|  | Sponsor: | Capital and Coast District Health Board |  |
|  | Clock Start Date: | 10 June 2021 |  |

Dr Maria Saito Benz 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 purpose of the study is to investigate in preterm babies, whether it is possible to keep brain oxygen levels in a specific target range for the first 5 days using a portable and non-invasive bedside monitor, Near Infrared Spectroscopy (NIRS), and following a dedicated clinical treatment guideline. Babies in this study will have either (a) the usual treatment (given to all babies), or (b) in addition to usual care their brain oxygen levels will be monitored using NIRS and clinicians will follow a dedicated treatment guidelines to aim to keen brain oxygen levels within target range during the first 5 days of life. 100 participants in two countries of which 20 will be New Zealand. Both arms have the NIRS sensor on the forehead, but the reading will be "covered" in the control group, and will alert doctor if outside reference range so adjustments can be made in intervention arm. Otherwise standard of care (i.e. ventilation support, CPAP mask/cap).

Summary of resolved ethical issues

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

1. The Committee was concerned about the emergency nature of pre-term deliveries and requested clarity on how the researcher planned to recruit antenatally versus postnatally while mitigating any further distress to mothers.
2. The researcher responded that the research team are also the clinicians on the ward and have significant experience in dealing with these types of situations including providing advice and answering any questions that parents may have about the study. The researcher added that the prospective mothers will already be on the antenatal ward prior to delivery and this is when the prospective parents will be approached to provisionally consent (antenatally).
3. The Committee advised that while they may obtain provisional consent antenatally this, legally, does not extend beyond the birth and therefore parents will be required to (re)sign a consent form after the baby is born. The Committee queried how this will work in practical terms (i.e. what documentation the parents will sign antenatally versus postnatally).
4. After some discussion around the legalities of consent, the researcher confirmed that parents will be provided with the Participant Information Sheet and Consent Form (PIS/CF) antenatally for information and should they verbally express their wish to continue, will be provided the PIS/CF again to sign postnatally (within 6 hours of delivery). She added that while they will speak to both parents about the study antenatally to gain provisional consent, they can obtain signed confirmation of consent from either the mother or the father after the baby is born.
5. The Committee acknowledged the researcher’s confirmation that the (antenatal) wishes of parents who do not want to be involved in the study are respected postnatally.
6. The Committee noted the statement in the protocol that a waiver of consent has been approved for recruitment purposes reflects the Australian legal context and acknowledged the researcher’s confirmation that there are no plans to enrol participants under a waiver in New Zealand.
7. The Committee asked what experience the researcher had with randomised control trials as this was not evident in the CV that was submitted. The researcher responded that while this is the first time she has taken part in a multi-centre trial, she has been involved in a randomised control trial previously looking at 60 elective blood transfusions in pre-term infants.
8. The Committee queried why the word ‘pandemic’ was listed as a reason for stopping the trial as stated in the PIS/CF. The researcher confirmed that the statement refers to recruitment being paused in Australia due to COVID-19, but does not anticipate recruitment being impacted in New Zealand.
9. The Committed noted the researcher’s explanation that the blinded randomisation element of the study refers to the reporting team undertaking the statistical analysis and clarified that the clinicians will not be blinded.

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 equipoise of the study and whether the cohort where the monitor readings are masked to the clinical team may be disadvantaged. For example, the O2 level readings if not missed/uncommunicated may have prevented a brain injury with a life-long impact. The researcher advised that infants are not being disadvantaged in the study as this type of monitoring is not being done in New Zealand as standard of care. She added that it is not used here as standard of care because there is no evidence to support improved outcomes which is why they are conducting this feasibility study to establish if there may be some benefit or not.
2. Following the researcher’s response, the Committee requested the information in the PIS/CF on benefits is neutralised and expanded upon to make the point that benefits are not known clearer to parents (i.e. that there is no evidence to support any benefits and that in fact, there may be some risks associated with being involved in the study).
3. The Committee advised that the PIS/CF does not have sufficient information regarding data. Please review the [HDEC’s PIS/CF template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc) 'What happens to my information section' and incorporate relevant components into the PIS/CF. Please address the collection and type of follow up information over the five years (e.g. MRI and videos), future use of data, sending data overseas, length of storage (26 years), collecting data from the ANZNN database, and linking to other health information. Please also ensure the information is consistent with the Data Management Plan.

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

1. Please update the data section as per the Committee’s previous point.
2. Please add an optional clause for future unspecified research to the consent form with yes/no tick boxes.
3. Please provide more information about how the risk of skin irritation is being mitigated, monitored and managed to provide parents with reassurance.
4. Please explain the purpose of randomisation in section 3 (i.e. that it is 1:1, that it is by chance (not toss of a coin), and to remove bias the doctor is not selecting).
5. In section 10, please write out ‘Health and Disability Ethics Committee’ in full and use the standard statement for HDEC approval in the [PIS/CF template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc) available on the HDEC website.
6. Please change the wording from ‘baby's disease’ to ‘baby's health’.
7. Please consider removing the optional withdrawal form as consent to withdraw does not need to be given in writing in New Zealand and can be given verbally.

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).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Mrs Stephanie Pollard and Ms Susan Sherrard.

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| **4** | **Ethics ref:** | **21/NTB/158** |  |
|  | Title: | A study to assess the safety and activity of a single injection of UBX1325 in patients with Diabetic Macular Oedema |  |
|  | Principal Investigator: | Dr Narme Deva |  |
|  | Sponsor: | Pharmaceutical Solutions Ltd |  |
|  | Clock Start Date: | 10 June 2021 |  |

Dr Narme Deva, Jessie Kane, Laruen Masaki, Paul Hamilton, Sharon Klier, Fiona Menzies, Aine Tyson-Flynn, Pam Tsuruda, and Deepa Parthasarathy 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 study is intended to assess the exposure, safety, and biological activity of UBX1325, a phosphate pro-drug, and its active parent molecule (UBX0601) following a single intravitreal (IVT) injection of UBX1325 in patients with diabetic macular oedema (DMO) that is refractory to existing therapeutic options. 3 countries with 62 participants including 5 from New Zealand.

Summary of resolved ethical issues

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

1. The Committee queried how effective the ‘no injection’ sham treatment is for a blind trial. The researchers advised that they have conducted the previous studies this way where the clinicians do an impression of giving an injection for the sham arm. She added, however, that an experienced patient would likely be able to tell the difference between receiving the intervention and receiving the sham.
2. The Committee queried how the researchers will achieve equitable access to this clinical trial if it is conducted in a private facility. The researchers advised that the intention is to enrol participants from as large of a population base as possible and she is therefore recruiting from other Auckland District Health Board (ADHB) sites including Waitakere, North Shore and Counties Manukau.
3. The Committee informed the researchers that in New Zealand a therapeutic study cannot be stopped simply for reasons of commercial interest. The Committee stated their preference that this option is removed from study documentation. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.37).*

Summary of outstanding ethical issues

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

1. The Committee advised that the specific locations and process for recruitment were missing and requested this is detailed more clearly in the protocol.
2. The Committee added that while the researchers can advertise widely through the clinics, they will be required to obtain authorisation from each of the (ADHB) clinics prior to approaching patients to recruit them for a study, irrespective of how or who is recruiting patients. This authorisation process is called a locality review.
3. The Committee noted the researchers’ confirmation that they will not be prescribing prophylactic antibiotics and recommended removing this from section 6.4 of the protocol.
4. The Committee suggested that given this drug has not been tested on many people, it is worth considering building in safety to the protocol, by adding reasons for stopping the study, to ensure participants are well protected in the event of unexpected safety issues.
5. The Committee noted that there were inconsistencies between the protocol, data management plan, and the PIS/CF on if tissue samples will be destroyed at the end of the study or if they will be used for future research. The researchers confirmed that samples will be used for the trial only in New Zealand and that further research refers to the PK samples only. The Committee requested that the researchers clarify this in 9.6 of the protocol.

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

1. The Committee noted that the PIS/CF states that participants may have difficulty driving home and that this ‘will be discussed’. Please state clearly in the PIS/CF if participants will be required to bring someone with them to drive them home or get a taxi, including if taxi chits will be supplied.
2. Please add the rescue protocol to the PIS/CF to provide participants with reassurance that they will not be disadvantaged in this trial (e.g. that the standard of care treatment will be maintained for participants during the trial).
3. Please add the permitted concomitant treatments for the study eye (e.g. artificial tears, antibiotics, etc.) and explain any limitations on treatment which includes to the non-study eye that is detailed in section 6.8.1 of the protocol.

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee
* Please update the Participant Information Sheet and Consent Form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, 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).*

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| **5** | **Ethics ref:** | **21/NTB/159** |  |
|  | Title: | Handheld thermal pulsation vs standard of care for MGD management |  |
|  | Principal Investigator: | Professor Jennifer P Craig |  |
|  | Sponsor: | The University of Auckland |  |
|  | Clock Start Date: | 10 June 2021 |  |

Professor Jennifer Craig and Ms Catherine Shon 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.

Leesa Russell declared a potential conflict of interest on the basis that she works with Professor Craig as she is a member of an ethics committee at the University of Auckland. The Committee decided that there was no conflict for this study, and she could participate in the discussion.

Summary of Study

1. This is a prospective, randomised, investigator-masked, parallel group, controlled clinical trial. People who suffer from dry eye disease frequently complain of irritated, burning and gritty eyes. Common reasons for this include a reduction of the tear film lipid layer due to the eyelid glands malfunctioning (meibomian gland dysfunction). Thermal pulsation therapy, introduced over a decade ago, offers such potential by allowing higher temperatures to be reached at the meibomian glands by applying the heat to the inner surface of the eyelid, and it combines the heat application with concurrent gland expression. The iLux® (Alcon) is a novel handheld, thermal pulsation device convenient for clinicians to incorporate into their dry eye practice.
2. This trial aims to explore the efficacy of the handheld thermal pulsation device in relieving the signs and symptoms of evaporative dry eye disease secondary to meibomian gland dysfunction of varying severity. The researchers would like to evaluate the ability of the device (currently available on the commercial market outside New Zealand) to improve tear film stability and thereby reduce symptoms of dry eye. Specifically, the researchers would like to look at the clinical course of ocular benefits, including how quickly improvements in signs and symptoms occur, the time taken to reach maximal treatment effect and the duration of effect. The researchers would also like to learn whether the outcomes are more successful compared to current standard of care (daily patient-applied warm compresses and gland expression).

Summary of resolved ethical issues

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

1. The Committee noted that the iLux® is expensive and asked the researchers to explain how it may become a cost-effective solution. The researchers stated that the iLux® is cheaper than the current treatment available in New Zealand, the LipiFlow. The LipiFlow currently costs approximately $1,000 per eye for treatment and is a large device. The iLux® is a handheld device and not currently marketed in New Zealand. It is not clear yet how much the iLux® will cost but it takes up less space than the LipiFlow. As the iLux® is smaller, more practitioners can use it and it would become a cheaper and more cost-effective treatment for patients.
2. The Committee asked the researchers whether the study is being conducted for the primary benefit of the manufacturer. The researchers clarified that the study is investigator-led. The manufacturer will not receive the study data and the research will be published by Professor Craig.
3. The Committee asked if the researchers will do the analysis themselves and they confirmed this will be done internally.
4. The Committee asked if participants will take the iLux® home. The researchers stated that participants will not be able to take the iLux® home. However, the warm compresses and gland expression that are standard care are applied by patients at home.

Summary of outstanding ethical issues

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

1. The Committee suggested that the researchers use the [HDEC Participant Information Sheet and Consent Form template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-sep20.doc) for the data section and compensation section of the Participant Information Sheet. Please amend those sections accordingly. Please also use the template for any future research applications.
2. The Committee noted that the Participant Information Sheet refers to contacting Heads of Departments (HoDs). The Committee advised that this is acceptable if recruitment is solely within the university. However, if there is any external recruitment, members of the public may not know who the relevant HoD is. Please include a statement such as, ‘if you are not employed at, or a student of, the University of Auckland, this does not apply to you’.
3. The Committee asked if the researchers will use advertisements to recruit participants. The researchers confirmed they will advertise through the University of Auckland using third party/Facebook advertisements. Please upload the advertisements for the Committee to review.
4. The Committee referred to the ‘study design’ section of the Participant Information Sheet that refers to participants being randomised to ‘the non-treatment group’. The researchers clarified that this should state ‘randomised to the standard of care’. Please amend this statement accordingly.
5. The Committee noted that the Participant Information Sheet and Protocol refer to destruction of clinical data after six years. The Committee advised that the HDEC requirement is 10 years. Please make this change throughout the documents.
6. The Committee noted that a separate Data Management Plan was not uploaded online. Please upload a copy of this document.
7. The Committee noted that there is reference in the Protocol to patients’ legally authorised representatives consenting on their behalf. Please remove this statement as this is not permitted under New Zealand law.
8. The Committee referred to a.1.6 of the application in regards to conflict of interest. Please state clearly in the Participant Information Sheet that both clinical care and academic progress will not be affected if participants decide not to take part.
9. The Committee referred to f.3.1 of the application that states participants will have access to the iLux® after the study ends. The Committee asked the researchers to confirm this. The researchers confirmed that participants who were not randomised to the iLux® for the study will have the opportunity to be treated with it after the study ends. Please include this information in the Participant Information Sheet if it is not included already.
10. The Committee referred to p.4.3 of the application and noted that the researchers indicated that there is no requirement for Māori consultation. The researchers stated that they partner with Māori, so all their research is reviewed by their Māori research partners. The researchers explained that they selected ‘no’ on the application because they do not require Māori consultation in the sense that they are not going directly to any marae or iwi to recruit participants. However, the researchers advised that the overall purpose of the study and the way they collect data, approach prospective participants, and report data is in collaboration with Māori. Please note that for future applications that unless the study excludes Māori from participation, consultation is always required.

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

1. Please identify the sponsor on the front page.
2. Please put the correct reimbursement sum to reflect that participants will receive $20 vouchers per visit and that there will be approximately seven to eight visits.
3. Please include tikanga in regards to touching participants’ eyes.
4. Please add page numbers to the document.

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. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Mr John Hancock and Mrs Stephanie Pollard.

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| **6** | **Ethics ref:** | **21/NTB/161** |  |
|  | Title: | SCIENCE |  |
|  | Principal Investigator: | Dr Nichola Wilson |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 24 June 2021 |  |

Dr Nichola Wilson 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 SCIENCE study is trying to improve the treatment of children who have a broken bone in the elbow called an ‘epicondyle fracture’. In New Zealand, and around the world, doctors treat these injuries in different ways. Half of doctors advise to rest the elbow in a cast or splint and allow it to heal by itself, whilst the other half advise surgery to fix the bone. Despite the number of these injuries, doctors are not sure whether one way of treating them is better than the other because it has never been researched.
2. This study, which is led by the University of Oxford in the United Kingdom, will compare the two commonly used treatments in a group of 334 children aged between 7 to 15 years old:
3. Resting the arm in plaster cast for up to 4 weeks, to allow it to heal by itself.
4. Surgery to fix the bone, usually with a screw and resting the arm in a splint or cast for up to 4 weeks.
5. All patients will then be followed up in hospital and get rehabilitation according to the usual practice of the treating hospital, which will include advice about moving the arm, and may include physiotherapy.
6. Participants will have this type of broken bone, and their doctors in the hospital will invite the children to take part in the study. There will be 25 participants recruited 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 that children will be in significant pain after breaking a bone in their elbow. The Committee asked how participants will be recruited in a way that gives them time to think about the study and assess risks and benefits for themselves. The researcher stated that children will often have had urgent care somewhere else. By the time they are seen by the researcher, they are usually more comfortable and will have been put in a back slab or resting plaster and had pain relief. Participants will have time to consider participation because they do not require an emergency procedure. Any child that requires surgery in theatre immediately is not eligible for the study.
2. The Committee asked if there is selection bias in terms of surgery outside the research setting. The researcher stated that it is more consultant-dependent rather than selection bias. Consultants discuss at meetings whether to proceed with surgery for patients. The decision on whether to operate or treat the bone in plaster is not often clear.
3. The Committee asked if participants will be contacted directly once they turn 12 years old. The Committee noted that the Consent Form states that children over 12 years old will give consent to be contacted directly and have their own phone/email. The researcher stated that despite this, it would be unusual in the setting to send information directly to the 12-year-old participant so they will send an email link to the parents’ email address instead. The Committee noted this is fine and the instructions do suggest that participants who are 12 years old should still go through the information with their parents.
4. The Committee noted that the sponsor is located in the United Kingdom and asked who will be responsible in New Zealand for the organisation, study conduct, and coordinating. The researcher stated it is the Starship Foundation; however, the Committee noted that they are a charitable foundation who do not conduct research. The researcher stated that under the Starship Foundation, there is a Starship research hub. The Committee noted that Auckland District Health Board (DHB) has two research offices so Auckland DHB/Starship will be the New Zealand sponsor.
5. The Committee asked how the researcher will manage being the treating clinician and the researcher. The researcher clarified that she is no longer a treating clinician and no longer does on-call work. She will not be involved in any of the surgeries.
6. The Committee asked if all participants will be able to get surgery if the study procedure is proven to be best treatment, and if the hospital is prepared for this. The researcher stated that if it is shown to be best treatment, it is hoped that hospital resources and space will be available. While this has not been planned for in advance, it will likely be workable.
7. The Committee asked if participants can be pulled out and given surgery if treatment is not going well, or if they must wait the full four weeks. The researcher explained that during the cast period, it cannot be identified whether treatment is not going well. A non-union would not be identified until after the cast period is finished. The Committee asked if there is a detriment to being in the cast group. The researcher stated there is no detriment as it is standard care.
8. The Committee noted that 15.5 of the Protocol refers to the Australian Ethical Standards, and that in New Zealand, research is conducted under the NEAC National Ethical Standards 2019.

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 researchers provided an assent form for children aged 7 to 15 years old. However, there is a literacy difference within that age range. Please provide separate assent forms for children aged 7 to 11 years old, and 12 to 15 years old. Please also make the forms specific to New Zealand with New Zealand contacts. It is also important to inform children that they can talk to their parents/whānau before they make a decision, and that if they do not participate in the study, they may still need treatment including surgery or a cast.
2. The Committee asked how the researcher will tailor the study to Māori given that a lot of the engagement and consultation work was completed in the United Kingdom. The Committee also noted that the researcher conducted an audit that showed that Māori will be a prominent group in the study. The researcher stated that they consulted with Ngā Rata K**ō**iwi which is the Māori health group part of the New Zealand Orthopaedics Association. They discussed the Participant Information Sheet and documentation and the group is supportive of the study. The study was also reviewed by Te Kupenga Hauora Māori (TKHM). TKHM provided feedback on the study and their main concern was around data and data sovereignty. The researcher stated that participant ethnicity data is not sent to the United Kingdom. The Committee noted that keeping identified and de-identified information is important in this regard. This also links to the Committee’s points about the Consent Form and encouraging participants to talk to whānau.
3. The Committee requested that the researcher provides a Data Management Plan, particularly with regards to Māori data sovereignty, who is getting what data, and how data will be shared. Please refer to the [HDEC Data Management Plan template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/data-only-management-template-oct2020.docx).
4. The Committee asked if all consent paperwork/process is on the website and how this will work. The researcher shared her screen with the Committee during the Zoom meeting to display the study website. The researcher stated that they have funding for iPads plus free Wi-fi throughout Starship Hospital. Participants may also use their own devices to access the website as it is freely available and can be accessed at other times too. Participants will receive a printed copy of the information. The Committee noted that the website is currently not specific to New Zealand, for example it refers to the British Pound instead of the New Zealand dollar. The researcher stated that the website will be updated and made specific to New Zealand and the consent forms will be added to it. The Committee asked if the information that will be updated on the website is the same as the information provided to the Committee. The researcher stated that the consent and assent forms are identical but there will be information such as videos for participants that the Committee has not seen. The Committee requested that the researcher formally provide a link to the website for it to review after the website has been made specific to New Zealand. Please also provide print-outs of the final website version so the Committee knows which version it approves. Please also send copies of the video(s) – a transcript is not required.
5. The Committee noted that trial numbers are included on the Consent Form. This is not usual in the New Zealand research context. In New Zealand, identifiable information is kept separate from de-identified information, such as trial numbers. The Committee asked the researcher to discuss this with the research team in the United Kingdom as there is a potential risk of participants identifying which participant they are in their dataset based on the provision of their trial number. The Committee asked if the researcher will put names on consent forms as well as study numbers. The researcher was not certain as to what the document looks like once printed. The Committee requested reassurance that the documentation, when printed, will not contain both the study number and participant name.
6. The Committee referred to 7.1 of the protocol and noted that the study’s adverse event management is based on Severity Assessment Code (SAC) events. The Committee explained that these are the criteria that hospitals and service providers use to manage adverse events. It is not the criteria that clinical trials use to manage adverse events. The study requires adverse event and adverse event coding, which are different to SAC events and SAC coding. The Committee suggested that the researcher should seek advice on how to manage adverse events and add this information to the protocol. Please also provide criteria about what will be included and excluded. The Committee also suggested that MEDrAS coding may be useful for the study.
7. The Committee requested an independent peer review of the study. Please refer to the [HDEC Peer Review template](https://ethics.health.govt.nz/assets/Uploads/HDEC/hdec-peer-review-template-june-2021.docx) for guidance.
8. The Committee referred to b.4.4.1 of the application and explained to the researcher that future data will be de-identified, not anonymous, given they will have key codes. Please keep this in mind for any future applications.
9. The Committee referred to r.2.4 of the application and noted that ‘de-identified’ should have been selected instead of ‘potentially identifiable’.

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

1. Please remove the comment bubbles from the documents.
2. Please include New Zealand contacts and sponsors’ details.
3. Please move the compensation provisions to the body of the ‘What happens if I get injured?’ section of the Consent Form. Currently, this information appears after the contact details.
4. Please make the information specific to New Zealand and state that the New Zealand research team is working with Oxford Trauma in the United Kingdom. Please also state that the website is run in the United Kingdom but the study is international.

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. *(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 Ms Susan Sherrard and Mrs Leesa Russell.

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| **7** | **Ethics ref:** | **21/NTB/162** |  |
|  | Title: | Comparison of a combination oral suspension containing paracetamol and ibuprofen in healthy volunteers. |  |
|  | Principal Investigator: | Dr Noelyn Hung |  |
|  | Sponsor: | Aspen Australia |  |
|  | Clock Start Date: | 24 June 2021 |  |

Dr Noelyn Hung and Linda Folland 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 bioequivalence study evaluating the rate and extent of absorption of the test formulation, a combination 250/100 mg paracetamol/ibuprofen oral suspension (Aspen, Australia) relative to that of two reference formulations administered simultaneously, 250mg Dymadon® oral suspension (Aspen, Australia) and 100mg Nurofen® oral suspension (Reckitt Benckiser, Australia) in healthy male and female subjects under fasting conditions. A single dose of the combination oral suspension and a single dose of the paracetamol and ibuprofen oral suspension administered simultaneously will be compared in this study.
2. The duration of the study is approximately five weeks, including up to three weeks for screening and nine days on study (two periods of one-day dosing with at least seven days of washout between each period).
3. Subjects will stay at the Zenith Clinical Site from 12 hours before dosing until approximately 14 hours after dosing in both study periods.
4. During one treatment period, the enrolled and randomised healthy subjects will receive a single dose of 10mL paracetamol/ibuprofen oral suspension and in the other treatment period will receive 1 x 5mL paracetamol oral suspension and 1 x 5mL Ibuprofen oral suspension oral liquid administered simultaneously taken in a fasted state. The dose in both periods is 250mg paracetamol and 100mg ibuprofen.
5. PK blood samples will be collected at baseline (before dosing) and at specified times up to 14 hours after dosing (total of 19 blood samples in each study period). The plasma will be assayed for paracetamol and ibuprofen using a fully validated LC MS/MS method.
6. Post-study exit procedures including laboratory tests, vital signs and safety assessments will also be carried out and subjects will be monitored for adverse events throughout the study.

Summary of resolved ethical issues

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

1. The Committee noted that the researchers requested a closed meeting for consideration of their application. The Chair declined the request. The Chair explained that the technical details that are transferred to the public-facing minutes are no more technical than would be in the Participant Information Sheet or Clinical Trials Registry. An open meeting would not disclose a trade secret or prejudice the company in any way. The researchers stated that the sponsor had requested a closed meeting but confirmed they had authority to proceed with discussion in an open meeting. Only the Committee, the researchers, and members of the HDEC Secretariat were present for the discussion.
2. The Committee noted that the study involves a new medicine and asked if the researchers had approval from the Standing Committee on Therapeutic Trials (SCOTT). The researchers confirmed that SCOTT approval had been received.
3. The Committee asked if the researchers will use different advertising and social media to that provided. The researchers confirmed they will not, apart from putting the advertisement outside their office wall, on Facebook, or on their website, but the wording will not change.

Summary of outstanding ethical issues

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

1. The Committee asked if the researchers have a universal trial number. The researchers stated they had not received this yet but confirmed they had applied. Please supply this when it is available.
2. The Committee noted that New Zealand is not named as a policy territory in the insurance certificate. The Committee requested confirmation that New Zealand is specifically included under jurisdictional limits.
3. The Committee noted that the insurance starts in September 2021, which is after the trial is planned to finish. The Committee asked the researchers to contact the insurance company and have the date advanced. Please provide a copy of the updated insurance certificate as a post-approval amendment.

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

1. Please add fluid restrictions in addition to fasting restrictions. For example, no water prior to dose for one hour as part of fasting restrictions.

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee
* Please update the Participant Information Sheet and Consent Form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*

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| **8** | **Ethics ref:** | **21/NTB/163** |  |
|  | Title: | Development of imaging biomarkers for prostate radiotherapy treatment response |  |
|  | Principal Investigator: | Dr Hayley Reynolds |  |
|  | Sponsor: | University of Auckland |  |
|  | Clock Start Date: | 24 June 2021 |  |

Dr Hayley Reynolds and Arpita Dutta 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.

Leesa Russell member declared a potential conflict of interest on the basis that she has a close working relationship with Dr Reynolds at the Auckland Bioengineering Institute. However, she was not specifically conflicted in relation to this study. The Committee decided that she could participate in the discussion.

Summary of Study

1. The purpose of this study is to analyse magnetic resonance imaging (MRI) taken before and after standard radiotherapy for prostate cancer to see how a patient is responding to the radiotherapy treatment. Currently, response to treatment is monitored using blood tests, to assess the level of prostate specific antigen (abbreviated as PSA) in the blood. After successful radiotherapy treatment, the PSA level should decrease and stay low. If the PSA does rise past a certain level, or if there are three consecutive rises, then the patient is considered as having a biochemical recurrence (meaning the cancer has come back). If only a PSA test is used, it is difficult to determine the cause of the PSA rise, whether this is due to the cancer returning or the PSA rising due to a non-harmful effect.
2. The aim of this study is to look at how MRI could help to monitor and assess treatment response. The additional MRI obtained during this study will be compared with blood test results, including levels of PSA and measures of oxygen which can impact response to radiotherapy. The researchers will also assess measures of oxygen level in prostate biopsy tissue already collected during standard of care procedures before treatment and compare this with the MRI information.
3. The results from this study will be combined with a larger study conducted at the University of Sydney, to help determine whether MRI could indicate response to treatment earlier than blood tests currently allow. If MRI can do this, then it would enable clinicians provide earlier interventions for prostate cancer patients if it is needed, to increase the chance of cure.

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 about the potential for gadolinium to stay in the brain after multiple MRIs. The researcher stated that it is a key ethical issue to ensure that patients know that gadolinium can deposit in the brain and remain there. The researcher stated they are not a MRI physicist but there are no known harms of gadolinium depositing in the brain.
2. The Committee noted there will be archival tissue use and asked how this will be managed. The researcher stated that the whole block will be taken from Auckland Pathology then they would take extra sections and send the block back but keep the sections that they have cut for the immunohistochemistry and store that at the Auckland Regional Biobank (ARB). It is just the extra immunoslides that will be stored at ARB but the blocks go back to pathology. The Committee noted that it is important to consider that if the whole block is taken, this may limit participation in other trials.

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 the researcher to supply the study’s universal trial number when it is available.
2. The Committee noted that participants should be able to receive compensation for expenses. Page 8 of the Participant Information Sheet currently states that ‘additional travel, parking, and meal costs that are incurred because of the additional visits will be at the cost of the participant’. However, a general principle is that participants should not need to pay for research participation, particularly for research that is of no benefit to them. Please discuss compensation with the sponsor. A minimum of a $20 petrol voucher per participant is an example of reasonable compensation.
3. The Committee noted that there is an option to store the extra samples securely at the ARB and that the researcher provided a copy of the ARB information sheet and consent form. The Committee noted that the ARB information sheet and consent form has improved but it still does not meet HDECs’ expectations for biobank consent forms. The Committee advised that the researcher could use the ARB documents for the study but asked that they provide feedback to the ARB so that it can update its forms in line with HDECs’ expectations. This feedback includes that the ARB should not be collecting any data, including ethnicity data, on the consent form. The Committee also noted that negative consents should not be used on consent forms.
4. The Committee requested a Data and Tissue Management Plan that includes information about how tissue will be collected, when it will be collected, who it will be handed to, and how transitions will be managed. Further, it is important to be clear about what will be sent overseas. Please refer to the [HDEC Data and Tissue Management Plan template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/hdec-data-tissue-management-template-oct2020.docx) for guidance. Once complete, please also update the relevant sections of patient facing information and the protocol.
5. The Committee noted that prostate cancer is one of the lead mortality cancers for Māori men. The Committee asked if the researcher is seeking a representative sample of Māori amongst the 10 participants. The researcher stated she had not discussed this with   
   Dr Giuseppe Sasso, the radiation oncologist who will primarily be responsible for recruiting patients. The Committee suggested that the researcher consider recruiting a sample of Māori participants as Māori will be the main people coming through the clinic with prostate cancer. Further, if the study works well for Europeans but does not work for Māori and Pasifika, this can be limiting later so it is important to start early.
6. The Committee referred to the three options regarding Future Unspecified Research (FUR) in the Participant Information Sheet and Consent Form. The Committee stated that it is fine to refer to FUR here, but that FUR should also be in a separate consent form so that it is truly optional. While the option boxes are helpful, the Committee suggested removing option 3 and including a statement such as, ‘the study [nurse/doctor/coordinator] will now discuss the options for FUR with you and there is a separate form for this’.
7. The Committee referred to r.2.4.1 of the application and advised the researcher that the HDEC time requirement for destruction of study data and materials is after 10 years, not six years.

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

1. Please remove the ‘yes/no’ tick boxes on the Consent Form for anything that is truly not optional. For example, in regards to the options about future use of data and also informing participants’ general practitioners about any abnormal results.

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. *(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 Leesa Russell and Mr John Hancock.

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| **9** | **Ethics ref:** | **21/NTB/156** |  |
|  | Title: | Hearing loss and CMV |  |
|  | Principal Investigator: | Dr Holly Teagle |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 10 June 2021 |  |

Dr Holly Teagle 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 observational study will review clinical findings from multi-disciplinary evaluation of children who have significant hearing loss secondary to a Cytomegalovirus (CMV) infection. CMV is the most common cause of congenital hearing loss in children and often results in other neurodevelopmental delays and disorders. Clinical evaluations of hearing, speech and language, occupational therapy and physiotherapy, educational psychology and paediatric neurology were collected as part of a specialty clinic at The Hearing House, which is the cochlear implant centre for the northern part of New Zealand. This clinic was supported by the Freemasons Foundation with the purpose of increasing knowledge and awareness of CMV and to provide a clinical service to families of children who have received cochlear implants. Four clinics were completed over a period of 12 months and included children from age two to 16 years and their family and whānau.
2. The aim of this study is to review the clinical data collected during these clinics, which includes reports from professionals in all the areas mentioned above, and to identify the range and prevalence of special needs in the areas of hearing, speech, language, fine and gross motor skills, psycho-social development, education, and general development for children who have undergone cochlear implantation after suffering hearing loss as a result of a CMV infection.

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 is a retrospective audit of data that has already been collected by the Hearing House. The Committee asked whether the study is part of quality assurance directed by the Hearing House or if the researcher is adding some prospective data collection and linking medical records. The researcher stated that the study is not for quality assurance and it started as a clinical project which was funded by the Freemasons as a special event. A multidisciplinary clinic with a cohort of patients already seen at the Hearing House was invited. It was completed in four different clinics and age groups. It is not a typical service that the Hearing House has offered before. The researcher added that the study is about a sensitive topic hence why informed consent is being obtained. The Committee commended the researcher for pursuing informed consent.
2. The Committee asked if the questionnaires uploaded to the Portal were all part of the funded special event and the researcher confirmed this.
3. The Committee asked if the researcher considers that participation may be induced due to families’ gratitude given that there was a prior special event funded by a charity. The researcher stated potential participants are part of their client base who they see on a regular basis.
4. The Committee asked if the study will be linked to any other data such as hospitals or general practitioners’ data. The researcher stated that because the children were referred to and seen by the Hearing House, they have a lot of background information that formed part of their clinical records upon presentation. The Committee noted this is less complicated in that no traditional data linking will be undertaken.

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 protocol is not sufficient, and it was difficult to review the study without a properly documented one. The Committee suggested that the researcher refers to the [NEAC National Standards 2019](https://neac.health.govt.nz/national-ethical-standards/) for detail about what an acceptable protocol looks like. Please provide a properly documented protocol that is independently peer reviewed. (*National Ethics Standards for Health and Disability Research and Quality Improvement paras 9.7 and 9.7a*).
2. The Committee noted that the peer review provided is not sufficient. Please note that literature reviews do not form peer review for HDECs. For guidance on appropriate peer review, please refer to the [HDEC Peer Review template](https://ethics.health.govt.nz/assets/Uploads/HDEC/hdec-peer-review-template-june-2021.docx). *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.26).*
3. The Committee stated that usually a Data Management Plan is required. It is possible to include information about data in the protocol only with a robust section about what the data will be used for, how it is being stored, what exactly is being used, how long it will be stored for, security information, and whether data will be identifiable. While the Committee did not request a separate Data Management Plan, it referred the researcher to the [HDEC Data Management Plan template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/data-only-management-template-oct2020.docx) for guidance on what to include in the protocol. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15a).*
4. The Committee noted that the researcher did not make clear how data will be stored and shared. It also appeared that identifiers would be left on data. The Committee advised the researcher that data must be de-identified if it is being stored or shared. Please remove participants’ names and use key codes and keep a separate spreadsheet with participants’ names and key codes separate from the study data. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15a).*
5. The Committee noted that children aged from six months to 18 years old will be in the study. The Committee commended the researcher for requesting consent for participation. However, given that the study spans a wide age group, parental consent is required for children under 16 years old. While the researcher had submitted a Participant Information Sheet for parents, there was no Consent Form. Please provide a Participant Information Sheet and Consent Form for participants who are 16 to 18 years old. Please provide a separate Participant Information Sheet and Consent Form for participants under 16 years old. For younger participants, assent forms are required. Please split those into two separate forms – one for participants who are seven to 11 years old, and one for participants who are 12 to 15 years old (due to different literacy groups). The Committee noted that there may be developmental impairments in some children, so it would be guided in regards to what level of information the researcher considers appropriate for the patient population. The Committee suggested keeping information simplified, and that use of visuals/pictures are helpful as well as tick boxes plus a signing page. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.19).*
6. The Committee asked the researcher to identify the study sponsor. The researcher stated that she is a professor at the Department of Audiology at the University of Auckland but does all of her clinical work at the Hearing House. The Committee advised that the sponsor would have overall responsibility of reporting to the Committee if anything goes wrong. The Committee asked the researcher to seek clarification from the Head of Department as to who the sponsor is, and provide this information when known. *(National Ethical Standards for Health and Disability Research and Quality Improvement, paras 9.8 and 11.1).*

Decision

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

## General business

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

|  |  |
| --- | --- |
| **Meeting date:** | 03 August 2021, 12:00 PM |
| **Meeting details:** | 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 4:45pm.