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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 20 June 2023 |
| **Zoom details:** | 965 0758 9841 |

| **Time** | **Review Reference** | **Project Title** | **Coordinating Investigator** | **Lead Reviewers** |
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| 12:30pm - 1.00pm | 2023 FULL 18044 | 3D human cancer models for drug discovery & therapeutic applications | Associate Professor Jaydee Cabral | Dr Kate Parker & Ms Catherine Garvey |
| 1.00pm - 1:30pm | 2023 FULL 13812 | The CIRCA DIEM Study | Dr Maria Saito-Benz | Mr Jonathan Darby & Dr Sotera Catapang |
| 1.30pm – 2:00pm | 2023 FULL 17829 | P-ICECAP | Dr John Beca | Mr Derek Chang & Ms Catherine Garvey |
| 2:00pm – 2.30pm | 2023 FULL 13126 | MoST CIRCUIT | Dr Jane So | Mr Jonathan Darby & Jade Scott |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Mr Derek Chang | Non-lay (Intervention studies) | 08/07/2022 | 08/07/2025 | Present |
| Dr Kate Parker | Non-lay (Observational studies) | 11/02/2020 | 11/02/2023 | Present |
| Dr Andrea Forde | Non-lay (Intervention studies) | 22/12/2021 | 22/12/2024 | Present |
| Ms Catherine Garvey | Lay (the Law) (Chair) | 19/03/2019 | 19/03/2022 | Present |
| Dr Sotera Catapang | Non-lay (Observational studies) | 11/02/2020 | 11/02/2023 | Present |
| Mr Jonathan Darby | Lay (the Law/Ethical and Moral reasoning) | 13/08/2021 | 13/08/2024 | Present |
| Ms Jade Scott | Non-lay (Intervention/Observational studies) | 15/08/2021 | 15/08/2024 | Present |

## Welcome

The Chair opened the meeting at 12pm and welcomed Committee members, noting that no apologies had been received.

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 16 May 2023 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **2023 FULL 18044** |
|  | Title: | Three-dimensional human cancer models for drug discovery and therapeutic applications |
|  | Principal Investigator: | Associate Professor Jaydee Cabral |
|  | Sponsor: | University of Otago |
|  | Clock Start Date: | 07 June 2023 |

No Researcher 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 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 following about the application form submitted:
   1. Section B8 of the Submission refers to participants having access to treatment after the end of the study. This is not further explained in the context of this study. Please clarify whether participants will have any direct access to study related interventions following the end of the study.
   2. Section B12 refers to MBIE funding application for peer review and the He Taonga Tapu Cancer Society Tissue Bank applications. Please provide evidence of peer review, including any issues raised by peer reviewers and the responses to this. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.26).*
   3. Section B17indicates that participants will have access to results. Please clarify what results may be available.
   4. Section C3.3 has been answered "Yes" to Kaupapa Māori methodology. Please clarify whether this is incorporated into the current study design. An amendment may be submitted following the planned consultation.
   5. Recruitment is not sufficiently well explained. The submission refers to the Dunedin Colorectal Cancer Cohort but has no explanation of who will be approached, how and by whom. Please also explain whether you intend to request archival or prospectively collected tissue and data or a combination of these.
   6. Section D4 states that participants will be identified “numerically”. This question relates to identification for recruitment purposes, not (de)-identification purposes. Please amend.
   7. Section E1 states there are no potential risks. This cannot be assessed from an ethical standpoint without further information about participant involvement. Please clarify.
   8. Section E4 acknowledges the possibility of incidental findings of clinical significance. Please provide further information regarding this possibility and how incidental findings will be managed.
   9. Section E8 indicates that there are no criteria to terminate. Please amend.
   10. Section G1 asks what health information will be used or generated and the response refers only to BRAF+ patients being identified. Please clarify what data is collected for all participants and how is this analysed, stored and managed.
   11. Section G2 states that no data is to be stored in identifiable form. This is inconsistent with the stated intention to return results, provide incidental findings and the possibility of future study related benefit for participants. Please amend.
2. The Tissue Bank application is relied upon as evidence of peer review and to describe the tissue required for this study. The uploaded application to the Tissue Bank is incomplete-many sections have not been answered that are very relevant to HDEC’s ethical review. The application does not refer to the samples that are requested, the section on data management has not been completed and other sections such as funding and commercial partner information are also blank. Please review and provide a completed copy of the application. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.26, 14.13, 14.16).*
3. Please explain the process for disposal of the tissue/s after use in this study.
4. The Committee noted the following regarding Peer Review *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.26)*:
   1. Please provide evidence of the scientific peer review for MBIE funding.
   2. Please provide the completed Tissue Bank form.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF) *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17, 7.39)*:

1. The participant information sheet lacks detail about data collection, storage, and management. Please amend.
2. Please include reference to the fact that participants will not gain any commercial benefit from their involvement in the study.
3. Please include a timeframe for participants to withdraw, as they will be unable to withdraw their tissue after it has been utilised for study purposes.
4. Please review the risk section and ensure that this includes identifiable risks such as incidental findings, privacy breach.
5. Please include reference to ethics approval.
6. Please include a Consent Form- [please refer to the HDEC template](https://ethics.health.govt.nz/guides-templates-and-forms/participant-information-sheet-templates/)
7. Please provide a completed, study specific Data Management Plan. The uploaded version was a copy of the HDEC template with no additional information regarding this study.
8. Please include correct details of HDC advocacy.

**Decision**

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

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| **2** | **Ethics ref:** | **2023 FULL 13812** |
|  | Title: | Cognitive Improvement by early Restoration of cirCADian rhythms in very preterm Infants through Environmental Modification: The  CIRCA DIEM Study |
|  | Principal Investigator: | Dr Gillian Phillipson |
|  | Sponsor: | Telethon Kids Institute |
|  | Clock Start Date: | 07 June 2023 |

Dr Gillian Philipson 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 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 recruitment process and how the Researchers will approach potential participants in a sensitive way given their situation as parents of very pre-term infants. The Researcher explained their experience in research in this population; and that there would likely be an opportunity to discuss the research with parents prior to birth in some cases. After providing initial information parents will be provided with more detailed information from clinicians about their participation. The voluntary nature of participation is reinforced as is reassurance that the best possible care is given regardless of the decision to participate. The Researchers explained the reasons for distinguishing the timeframe for recruitment of participants with infants born at less than 28 weeks, and those born later.
2. The Committee asked for clarification of any differences between units in Australia where this trial originates, and New Zealand. The Researcher explained that there are differences between all units regardless of location and this is a driving factor in including New Zealand sites.
3. The Committee asked about timing of discharge and any implications for the cessation or continuation of the study intervention. The Researcher explained that discharge is fairly standardised in terms of discharge close to estimated delivery date, and clinically driven, not determined by involvement in the study.
4. The Committee asked which device is TGA class 1 in relation to this notation in the submission. The Researcher explained that the eye masks are Class 1 devices and are registered as such, however the use of these devices is ordinarily for short term treatment of photosensitivity and jaundice and is for a longer term and different use in this trial. The researchers plan for infants in the intervention group to wear the eye masks for every night for up to 12 weeks.
5. The Researcher confirmed that Māori consultation is currently taking place and will be addressed as part of locality authorisation.
6. The Committee asked for clarification of some of the exclusion criteria. The Researcher explained that the exclusions are for chromosomal abnormalities or significant neurological conditions that would require severe surgical intervention during the critical period shortly after birth. There will be a case-by-case discussion as to the suitability of enrolment for infants with abnormalities at birth.
7. The Committee asked about the sub-studies which will be conducted in New Zealand. The Researcher confirmed that the sub study involving biological samples will be in Western Australia only. The other sub studies will be offered to New Zealand participants. The researcher acknowledged there was room for discussion on when and how to present these, that is, within the main participant information sheet (PIS) or separately and had presented these in the main PIS based on feedback from Australian participants.
8. The Committee asked what plans are in place for follow up of participant responses to the study questionnaires. The Researcher explained that the questionnaires will be seen in a timely fashion and an alert system is in place with the ability to provide input from a clinical psychologist, and a range of services.

**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 insurance is also not New Zealand specific, please amend. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 17.1).*
2. The Committee requested the Researchers submit the updated study protocol. Any New Zealand specific amendments can be provided as a country-specific Appendix if that is considered appropriate. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).*
3. Please submit the easy-read pamphlets and the recruitment video.
4. Please include what congenital neurodevelopment abnormality’ are and give examples, also please clarify that participant’ will be excluded based on congenital neurodevelopmental abnormality and ensure that there is room for cases by case analysis of eligible infants.
5. Please provide the amended protocol with all the New Zealand sites, and reference to the planned satellite sites. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).*

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF) *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17)*:

1. Please provide a title for the first survey questionnaire (clinical epi).
2. Please specify in the protocol where recruitment in New Zealand will happen.
3. This study includes several sub studies, which are currently briefly described in the main PIS. Please either provide more information on each of the sub studies or provide separate information sheets. The information currently provided is insufficient.
4. Please ensure that the PIS clearly describes what data is collected, in what form, who has access to it, what it is used for and how long the data will be retained.

**Decision**

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

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| **3** | **Ethics ref:** | **2023 FULL 17829** |
|  | Title: | Paediatric Influence of Cooling duration on Efficacy in Cardiac Arrest Patients (P-ICECAP) |
|  | Principal Investigator: | Miss Claire Sherring |
|  | Sponsor: | The University of Michigan |
|  | Clock Start Date: | 07 June 2023 |

Dr John Beca 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 resolved ethical issues**

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

1. The Committee noted the likelihood that participants would be enrolled on the basis that this was in their best interests rather than prospectively consented and asked the researcher to discuss this in terms of the direct interests of the participants. The Researcher explained that the outcomes are poor with out of hospital cardiac arrest, with a high mortality rate, and a high rate of significant brain damage in survivors. The Researchers noted the available evidence in adults and neonates for cooling, and the need for evidence in children, and equipoise about current temperature management options. The Researchers noted differing practices between sites in Australasia, and that there is genuine equipoise with regard to temperature management in OHCA. The researcher noted that study and clinical staff are all familiar with temperature management in the relevant clinical scenario such that delivering treatment within the context of this study is well within their expertise.
2. The Committee asked when participants will be recruited, if it is possible to gain prospective informed consent, and the expected delay in discussing participation in those who may be enrolled on a best interests’ basis. The Researcher explained that they are required to exercise judgment given the situation potential participants will be in and that the delivery of information about the study may be incremental, but in those where there is no prospective consent, there is the intention where appropriate to raise the research within the first day after enrolment.
3. The Committee noted that one of the primary objectives of the study is assessed using the VABs-3, which is for English and Spanish speakers, and questioned whether this would influence the ability of New Zealanders who do not have English or Spanish as a primary language to participate. The Researcher explained that the protocol has come out of the US hence the use of this tool but did not anticipate any difficulties arising for NZ participants.

**Summary of outstanding ethical issues**

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

1. The Committee requested a New Zealand Peer Review.
2. The Committee requested a Data Management Plan that specifically addresses data collection, use and storage at the New Zealand sites.
3. Regarding section 4.6 of the protocol, please ensure that the intention regarding pregnancy testing in participants who are of childbearing potential is made clear and clarify if pregnancy testing will be done as routine care on admission to PICU in those of childbearing potential, and if not how is this managed.

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

1. Please consider simplifying the Participant Information sheets.
2. Please review for grammatical errors (e.g., on page 5 and 7).
3. On page 8 Authorities in New Zealand, please remove or amend if needed.
4. Please review and simplify the assent form for participants aged 12- 15.

**Decision**

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

1. Please address all outstanding ethical issues, providing the information requested by the Committee.
2. Please update the participant information sheets and consent forms, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
3. Please update the study protocol, taking into account the feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).*
4. Please supply a more detailed data management plan to ensure the safety and integrity of participant data. This can be a standalone document or incorporated as part of the protocol *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15a).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Ms Catherine Garvey and Mr Derek Chang.

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| **4** | **Ethics ref:** | **2023 FULL 13126** |
|  | Title: | Ipilimumab and nivolumab combination therapy in patients with selected immunotherapy sensitive advanced rare cancers |
|  | Principal Investigator: | Dr Jane So |
|  | Sponsor: | Olivia Newton-John Cancer Research Institute |
|  | Clock Start Date: | 07 June 2023 |

Dr Jane So 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 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 participants and the subgroups of rare cancer, and if recruitment is to be evenly split between each type of cancer. The Researcher explained that enrolment is on a basis of recruitment by eligibility regardless of rare cancer type, so there is no allocation of study places between the rare cancer categories under assessment.

**Summary of outstanding ethical issues**

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

1. The Committee requested clarification of the relationship between the MoST study and this study so participants know what elements of the testing is mandatory and what is optional. Please include information that clarifies the relationship between this and the MoST studies so that participants are aware what is necessary to determine their eligibility for this study, and what is optional with the prosect of future clinical trials based on their submission of tissue to MoST.
2. On page 4, please remove teaspoons as a form of measurement.
3. Please make clear that if a participant is receiving therapeutic benefit the sponsor will continue to provide access to nivolumab after they have completed the study.
4. Please check page numbering throughout the participant information sheet.
5. Please ensure that the PIS accurately describes the tumour assessments that are required and is consistent with the protocol,
6. Please ensure that the table on page 6 includes standard of care tumour assessments post week 18.
7. Please amend page 6 as to archival tissue testing and include if there are any risks associated with this, including the use of all the tissue. Please include the potential risks and cultural issues associated with sending and storing data and tissue overseas.
8. Please make it clear to participants what reimbursement is available.
9. Please include that a karakia will not be available if the tissue is stored and disposed of in Sydney.
10. Please remove the 0800 HDEC number and replace it with the one provided in the [HDEC template](https://ethics.health.govt.nz/guides-templates-and-forms/participant-information-sheet-templates/).
11. Please amend page 15 by changing biological testing to “genomic testing” to be more transparent.
12. Please include details for OMICO in the participant information sheet and the data management plan in the appropriate place.

**Decision**

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

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

After receipt of the information requested by the Committee, a final decision on the application will be made by Mr Jonathan Darby and Ms Jade Scott.

## General business

1. The Chair reminded the Committee of the date and time of its next scheduled meeting:

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| **Meeting date:** | 18 July 2023 |
| **Zoom details:** | To be determined |

1. **Review of Last Minutes**

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

1. **Matters Arising**
2. **Other business**
3. **Other business for information**
4. **Any other business**

The meeting closed at 3:00pm.