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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 01 December 2015 |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

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| **Time** | **Item of business** |
| 1.00pm | Welcome |
| 1.05pm | Confirmation of minutes of meeting of 10 November 2015 |
|  | New applications (see over for details) |
| 1.30pm | i 15/NTA/190  ii 15/NTA/194  iii 15/NTA/195  iv 15/NTA/197  v 15/NTA/198  vi 15/NTA/199  vii 15/NTA/200 |
| 4.25pm | General business:   * Noting section of agenda |
| 4.35pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Brian Fergus | Lay (consumer/community perspectives) | 01/07/2012 | 01/07/2015 | Present |
| Ms Susan Buckland | Lay (consumer/community perspectives) | 01/07/2012 | 01/07/2015 | Present |
| Dr Karen Bartholomew | Non-lay (intervention studies) | 01/07/2013 | 01/07/2016 | Present |
| Dr Christine Crooks | Non-lay (intervention studies) | 01/07/2013 | 01/07/2015 | Present |
| Ms Shamim Chagani | Non-lay (health/disability service provision) | 01/07/2012 | 01/07/2015 | Present |
| Dr Kate Parker | Lay (consumer/community perspectives) | 11/11/2015 | 11/11/2018 | Present |
| Dr Charis Brown | Non-lay (intervention studies) | 11/11/2015 | 11/11/2018 | Present |

## Welcome

The Chair opened the meeting at 1.07pm and welcomed Committee members.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

The Chair welcomed new members, Dr Charis Brown and Dr Kate Parker, to the Committee and noted the contribution of the members who have left the Committee. The Committee members introduced themselves and described their backgrounds and interests.

## Confirmation of previous minutes

The minutes of the meeting of 10 November 2015 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **15/NTA/190** |
|  | Title: | Molecular analysis of squamous cell carcinoma of the vulva and the field of cancerization |
|  | Principal Investigator: | Dr Susan Bigby |
|  | Sponsor: |  |
|  | Clock Start Date: | 19 November 2015 |

Dr Susan Bigby was present in person for discussion of this application.

Potential conflicts of interest

The Chair asked members to declare any potential conflicts of interest related to this application.

Dr Kate Parker declared a potential conflict of interest. The Committee discussed the potential conflict and decided to have Dr Parker take part in the discussion and decision of the application.

Summary of Study

1. The Researcher(s) explained that she is a pathologist at Middlemore Hospital, adding that the study involves collaborating with a multidisciplinary team.
2. The Researcher(s) explained that very little work has been done on tumours in the vulva. This study aims to identify the molecular events implicated in multistep carcinogenesis and define the risk field for cancers in the vulva. This will involve a comparison between primary and reoccurred tumours.
3. She will examine embedded tissue blocks. There are two parts to the study. Firstly she will use her expertise to identify microlesions for microsection with extract from these being sent for genetic marker analysis at Auckland University.
4. A range of genetic mutations implicated in SCCV will be searched using gene sequencing & gene expression.
5. To illustrate to the Committee the kind of archival tissue to be used in the proposed research and proposed tissue bank Dr Bigby tabled and presented a tray of laboratory cassettes and a series of laboratory slides containing human tissue samples.

Summary of ethical issues (resolved)

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

1. The Committee asked how cases are identified. The Researcher(s) explained potential participants are women with secondary precancers and cancers who will be identified from the records of the Auckland Regional Gynaecological Oncology Service. Committee asked how accurate this information was. The Researcher(s) stated that the data had been used for a similar purpose and proved accurate.
2. The Committee queried how potential participants will be approached. The Researcher(s) explained the women come in for ongoing surveillance at which point they can be offered to participate.
3. The Committee asked about the number of potentially eligible participants / samples. The Researcher(s) explained that because they have not yet searched for potential participants they are not aware of the numbers of participants who are potentially eligible.
4. The Committee asked how many cases of this cancer present annually. The Researcher(s) stated about 20 a year.
5. The Committee asked what proportion of women have recurrence with this form of cancer. The Researcher(s) stated about 20% with vulva cancer. The Researcher(s) could have to assess samples up to 10 years old, adding this was not ideal as DNA degrades over time.
6. The Researcher(s) stated most cancers reoccur within 2 years of clearance.
7. The Committee asked if the researchers are satisfied that the data generated will be representative of the patient cohort. The Researcher(s) stated they were.
8. The Committee asked for an overview of the consent plans for the study. The Researcher(s) explained they plan to seek consent from women in all possible cases. In cases of women who have died, their family will be approached to provide consent. The Researcher(s) anticipate cases where women have passed away and their family is not able to be contacted. In these cases the Research asked if the Committee is comfortable to provide approval for use of tissue without consent. The Committee was satisfied that for stored samples where patients had died, and where reasonable efforts have been made to seek consent of family, it was justifiable to use samples for this study without consent.
9. The Committee queried if any incidental findings from germline DNA work will occur, or whether patients would be identifiable from their DNA if Next Generation Sequencing were to be used, as cited as a possibility in the peer review. The Researcher(s) stated it is not likely that anything worth returning will be identified, noting that all patients are fully treated. Please be clear in the PIS that you will not be providing women with any results from the study.
10. The Researcher(s) noted there were no plans to send tissue overseas, even though this was stated in the submission.

Summary of ethical issues (outstanding)

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

1. The protocol requires information on the control group, consent mechanisms, how participants who have passed away will be identified in order to prevent unnecessary distress for families during the consenting process. Please update the protocol.
2. The Committee noted this study needs Maori review, contrary to the answer in the application. The Researcher(s) explained that the application answer was an error and that consultation was planned.
3. The Committee noted that there would be potential cultural issues. Māori and Indigenous people consider the body tapu. Researchers involved in health or medical research that involves the body, or any part of the body, such as organs, blood, hair, saliva and/or other tissue, must do so in a respectful manner. The collection of human tissue is particularly sensitive when it involves the use of a deceased person’s tissue. The response should discuss potential issues relating to tissue, in particular collective ownership of tissue or consideration of whakapapa etc if any sampling is done. This includes discussion of consent from iwi separate from individuals where appropriate (e.g. deceased individuals). Please review the Te Ara Tika guidelines for guidance.
4. The Committee asked for more information on the patient population. The Researcher(s) stated that they would identify women who had vulva cancer and have been fully treated, then once cured, have experienced reoccurrence. The samples are retrospectively accessed. The Researcher(s) added they planned to add a control group of women.
5. The Researcher(s) explained they required 20 cases and 20 controls. The Committee noted that the control group is not outlined in the protocol. The Researcher(s) explained that the idea for a control group resulted from a recent meeting. The Committee noted that the protocol will need to be updated and reviewed by HDEC prior to a final decision.
6. The Committee queried what happens to samples after analysis, noting that the application states the original embeded block will be returned to the original pathology laboratory, however the application also includes consent to future unspecified use storage that is not outlined or justified in the protocol. There is uncertainty about the samples going to Auckland University. The Researcher clarified that tissue could be stored in the Auckland Alliance tissue bank, but this requires clarification.
7. The Committee noted that any tissue that is stored beyond the length of the study constitutes tissue banking. Therefore the tissue must be stored in an established tissue bank that has HDEC approval. The Committee requires written evidence of an agreement between the researchers and an established tissue bank, otherwise tissue cannot be stored beyond the duration of a study. The committee requests a statement from Dr Shelling addressing the FUR issues specified below, particularly information about how long the testing of these is expected to take, whether some is biobanked for FUR using new markers etc. Please provide a timeframe for length of storage is expected in the response.
8. Furthermore, to seek consent for storage of human tissue for future unspecified research a participant information sheet must include the following:

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| **Future Unspecified Research (FUR) and Biobanking** |
| An indication of the type and nature of the research to be carried out and its implications for the donor, where possible, and an explanation of why the potential donor is being approached for their tissue and specifically what tissue is being sought. |
| Known possible researchers or institutions that might use the tissue sample, if possible. |
| Whether the donor’s sample is going to be, or is likely to be sent overseas, and where possible, to what country or countries. |
| Acknowledgement that all future unspecified research in New Zealand will be subject to ethical review. However, when a tissue sample is sent overseas, unless it is sent in conjunction with a New Zealand research project, future research is likely to be considered by an overseas ethics committee without New Zealand representation. |
| Whether the donor’s identity and details will remain linked with the sample or whether the sample will be de-linked. |
| A statement that if a donor consents to a tissue sample being unidentified or de-linked, they relinquish their right to withdraw consent in the future. |
| Whether the donor may be contacted in the future regarding their tissue sample. Whether or not, and under what circumstances, information about the future unspecified research will be made available to the donor and/or (where relevant) their clinician. |
| Acknowledgement that the donor will not own any intellectual  property that may arise from any future research. |
| Whether there is provision to withdraw consent for the use of human tissue samples in the future. Where there is provision to withdraw consent, only tissue samples remaining at the time of a request to withdraw and any information held for future unspecified research may practically be withdrawn. Tissue samples or information used in research before the request to withdraw is received is unlikely to be able to be returned or destroyed. |
| Acknowledgement that the donor’s decision regarding the consent for use of their tissue sample for unspecified future research will in no way affect the quality of a donor’s current or future clinical care. |
| Where and for how long a tissue sample will be stored, how it will be disposed of and whether there is a cultural protocol for its disposal. For example, information about the institution holding the tissue sample: its aims, research procedures and research governance. |
| Whether or not tissue samples could be provided to other researchers and institutions, and whether or not such provision could include sending samples to other countries |
| Whether or not collected samples will be provided to commercial biomedical companies or will be used in commercial research collaborations, if known. |
| What provisions will be made to ensure patient confidentiality. |
| That different cultural views may inform choice about donation of tissue; for example, for some Maori, human tissue contains genetic material that is considered to be collectively owned by whanau, hapu and iwi. |
| That cultural concerns may arise when tissue samples are sent overseas, including how tissue samples are stored and disposed of. Processes for monitoring and tracking what happens to samples may not be acceptable to donors. |
| That donors may want to discuss the issue of donation with those close to them, for example; family, whanau, hapu and iwi. |

For more information see the Guidelines for Future Unspecified Research <http://www.health.govt.nz/publication/guidelines-use-human-tissue-future-unspecified-research-purposes-0>

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

1. Please address the issues surrounding the tissue and whether the future unspecified research is restricted to research on cancer, or whether it is truly for any future unspecified research (i.e. biobanking).
2. Make it clear that the project does not require any additional tests for the women or any additional information. The study only involves existing tissue and access to health data. (page 2).
3. Clarify level of specimen identification when stored during the study and if stored for future research.

Decision

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

* Ensure the optional future unspecified research information sheet and consent form meets criteria set out in the guidelines (*Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes, para 2*).
* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Please justify the control arm. Provide an updated protocol outlining information on mitigating risk when recruiting, identification of deceased, identification of family etc. The study design should be the one best suited to answer the study question, while minimising harm, maximising benefit and meeting other ethical standards. (Ethical Guidelines for Intervention Studies para 5.4).
* Provide written evidence regarding where tissue will be stored after the study or for research purposes, noting that tissue banks must be registered with HDEC. (HDEC Standard Operating Procedures chapter 13)
* The Committee strongly urges the researcher to consult the appropriate Maori authorities to gain a thorough understanding of Maori issues surrounding the handling and use of tissue. The Committee will need the relevant correspondence seeing this has occurred and the approval of the Maori review committees involved.

This following information will be reviewed, and a final decision made on the application, by Dr Karen Bartholomew and Brian Fergus.

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| **2** | **Ethics ref:** | **15/NTA/194** |
|  | Title: | Safety and Efficacy of EXE844 Otic Suspension in OMTT |
|  | Principal Investigator: | Dr Murali Mahadevan |
|  | Sponsor: | Alcon Laboratories (Australia) Pty Ltd |
|  | Clock Start Date: | 19 November 2015 |

Dr Maayan Gruber (co-investigator) and Claire Perrott (sponsor) were present by teleconference for discussion of this application.

Potential conflicts of interest

The Chair asked members to declare any potential conflicts of interest related to this application.

No potential conflicts of interest related to this application were declared by any member.

Summary of Study

1. This is a Phase III study that aims to generate safety and efficacy data on study drug.
2. Study aims to show the study eardrops (Finafloxacin Otic suspension) are more effective than standard of care for treatment of infection after the insertion of Tympanostomy Tubes.
3. The Researcher(s) explained the different approaches of clinicians both within their own clinic, around New Zealand and internationally. The use of eardrops and their effectiveness meets the equipoise standard.

Summary of ethical issues (resolved)

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

1. The Committee noted that the study inaccurately stated there are no ethical concerns (a.1.6). Some examples are that the study involves potentially vulnerable participants, as some children can’t consent for themselves, and that it is a blinded study.
2. The Committee noted SCOTT review was pending.

Summary of ethical issues (outstanding)

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

1. The Committee noted study is blinded. Please explain how the study card will work, noting there is no contact information on it - if a child needed medical attention who would they contact? Does the Co-ordinating Investigator have unblinding rights, and is there a process for this? The Researcher(s) explained there is a first point of contact EMT who is on call 24/7, but was unable to explain the process for unblinding or any protocols in place.
2. The Committee requested a full plan for unblinding procedures in case of emergency.
3. The Committee asked whether the study would collect ethnicity information. The Researcher(s) stated yes. The Committee noted due to study being an international study it is likely that the standard data collection method will not be relevant for a New Zealand population. Please collect data using the New Zealand Census formats for consistency with national data collection. HDEC administration can provide advice on this
4. The Committee noted parents must also consent to participate, as they will be completing questionnaires. This can be incorporated into current parent Participant Information Sheet.
5. The Committee noted that the assent form (noted for use in 7-12 year olds) was too complex for a 7 year old. Please consider providing age appropriate assent forms.

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

1. Please note that some health information must be stored for a minimum of 10 years according to the [Health (Retention of Health Information) Regulations 1996](http://legislation.govt.nz/regulation/public/1996/0343/latest/DLM225650.html). For children it is 10 years after the date the child turns 16. Please include this information in the Participant Information Sheet.
2. Refer HDEC template Participant Information Sheet for ACC information.
3. Section 15 is usually at start of Participant Information Sheet. Please move for nz consistency.
4. The Committee noted that the wording in the Participant Information Sheet limited insurance for participants. If cover under the Accident Compensation Act 2001 will be excluded for the intervention study, investigators and study sponsors have responsibilities to ensure alternative compensation cover for study participants to at least ACC-equivalent standard. This requirement is an ethical standard set out in 8.4 of the National Ethics Advisory Committee Guidelines.
5. Remove ‘IRB’, waiving legal rights etc. This is not relevant for a New Zealand context.
6. The Committee noted Maori support details are a Waikato number, please ensure this is correct.
7. Amend the approving HDEC to NTA.
8. Review for jargon and explain technical terms in lay language.
9. Refer to ‘your child’ in the parent Participant Information Sheet as the child is the primary participant.
10. Please clarify (page 7) does not refer to identifiable data being sent to the sponsor. The Researcher(s) confirmed it was de-identified data that was sent to the sponsor. The Committee requested that this is made clearer in the Participant Information Sheet

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Please provide age appropriate information sheets and assent forms for younger participants and amend the existing information sheets and assent/consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Provide further information on the study design, *in particular the unblinding procedures* (*Ethical Guidelines for Intervention Studies para* 5.41)

This following information will be reviewed, and a final decision made on the application, by Dr Christine Crooks and Dr Brian Fergus.

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| **3** | **Ethics ref:** | **15/NTA/195** |
|  | Title: | Safety and efficacy of ziv Aflibercept compounding in refractory diabetic macular oedema |
|  | Principal Investigator: | Dr Andrew Riley |
|  | Sponsor: |  |
|  | Clock Start Date: | 19 November 2015 |

Dr Andrew Riley (CI) and Ms Sarah Welsh were present in person for discussion of this application.

Potential conflicts of interest

The Chair asked members to declare any potential conflicts of interest related to this application.

No potential conflicts of interest related to this application were declared by any member.

Summary of Study

1. The study investigates study drug in refractory diabetic macular oedema (a leading cause of blindness in patients with diabetes).
2. The Researcher(s) explained the treatment options available to patients, emphasising the very high cost of current best available treatment. The cost is unsustainable which limits its use for care.
3. This protocol uses compounding to reduce the costs from $2k per injection to $113 per injection. This will enable more patients to be treated.
4. Thus, the study drug will make treatment more accessible, and potentially increase length of time between required visits.
5. The study involves off label use of a drug (Aflibercept) which has an efficacy profile superior to the current standard treatment in New Zealand. The Researcher(s) confirmed this is a pilot to test an effective drug using a different formulation (compounded). The researchers have used the compounding process for a similar drug in a similar research setting which has become standard practice.

Summary of ethical issues (resolved)

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

1. The Committee asked about infection risks. The Researcher(s) explained there have been no infections in New Zealand when using compounding methods. General risk of infection is 1 in 1000 internationally, with New Zealand rates being 0.3 in 1000. This risk is present in standard of care, and is treatable.
2. The Researcher(s) noted 10% of patients are Maori due to the higher diabetic prevalence, with 50% of patients are Pacific. The Researcher(s) confirmed they had a consultation plan.
3. The Committee queried whether the serious adverse events and stopping conditions were clearly defined, and asked why 4 were cited as a stopping criterion. The Researcher(s) stated 1 in 200-300 could have inflammatory response to drug. If they saw 4-5 in first 40 it would be a good indication to stop the study. The Researcher(s) do not anticipate this response, however 10% of 40 is 4, which is where the number came from. The Researcher(s) confirmed this is in the protocol and safety data is reviewed every month.
4. The Committee queried if it was possible to provide post study access for participants who benefited from the treatment. The Researcher(s) explained it depends on outcomes from study. It could be possible to continue access through further studies, or it may be the case that this study shows the treatment is safe and the ADHB may allow compassionate or off label use in practice.

Summary of ethical issues (outstanding)

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

1. The Committee suggested using a study number rather than NHI. The Researcher(s) confirmed they would use a study number.
2. The Committee noted the study required a clinical trials reference number. See <http://www.anzctr.org.au/>

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

1. Add a table for participants that outline the number of visits and what occurs at each visit.
2. Please review the yes / no tick boxes on the consent form and remove those that are not actually optional to statements.
3. Add that participants can withdraw at any time. See the HDEC template Participant Information Sheet for guidance on what information to include. See this template for ACC information too.
4. The Committee noted the Participant Information Sheet repeats itself, and that this is due to the summary at the beginning. Please review
5. The Committee noted the reason for the font size of the Participant Information Sheet, but this was explained as due to poor eye sight of the participant, but please consider the HDEC template for structure and flow.
6. The Committee noted risk section on SAEs eg myocardial infarction, DVT, stroke requires context, or quantification.
7. Add information on infection rates, noting that New Zealand is lower than international averages.
8. Please explain jargon in lay language.
9. Explain why follow up and access to health information for outcomes is important, and have it as an option on the consent form.
10. Page 11, remove statement that HDEC will view participant’s health information, this will not happen.

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Make the changes suggested by the HDEC with regard to data confidentality and registration of study in a clinical trial registry.

This following information will be reviewed, and a final decision made on the application, by Ms Shamim Chagani and Dr Karen Bartholomew.

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| **4** | **Ethics ref:** | **15/NTA/197** **(CLOSED)** |
|  | Title: | A Phase IIb Study of NTCELL in Patients with Parkinson's Disease |
|  | Principal Investigator: | Dr Barry Snow |
|  | Sponsor: | Living Cell Technologies New Zealand Limited |
|  | Clock Start Date: | 19 November 2015 |

Dr Barry Snow (CI) was not available. Mark Simpson, Ken Taylor & Jenny Han in person were present in person 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.

Decision

This application was *provisionally approved* by consensus.

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| **5** | **Ethics ref:** | **15/NTA/198** |
|  | Title: | The Role of Lifestyle Factors in Breast Cancer |
|  | Principal Investigator: | Dr Rachael Flanagan |
|  | Sponsor: | NZ Breast Cancer Foundation |
|  | Clock Start Date: | 19 November 2015 |

Dr Rachael Flanagan (CI) and Dr Reena Ramsaroop were present in person for discussion of this application.

Potential conflicts of interest

The Chair asked members to declare any potential conflicts of interest related to this application.

Dr Kate Parker, Dr Christine Crooks, Dr Karen Bartholomew and Dr Charis Brown declared a potential conflict of interest, and the Committee noted the conflicts and decided to have members take part in discussion and decision of the application.

Summary of ethical issues (resolved)

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

1. The Committee noted the prior study had been declined.
2. The Researcher(s) explained that the study before the committee was entirely different from the declined study.
3. The Researcher(s) explained that the previous study was changed to a retrospective clinical data note review. This study involves a questionnaire that is given to all newly diagnosed patients at North Shore hospital. Based on the answers given they are assigned a risk factor. From this information they will try and optimise the patients health and wellbeing during their cancer journey.
4. The Researcher(s) explained that this study also aims to set up a long-term database to follow up 1- 5 years post diagnosis, collected anonymously, to relate it to the questionnaire. The data will be accessed for research once enough data is collected.
5. The Committee asked if The Researcher(s) are satisfied that the new questionnaire has a ‘no blame’ approach of patients (as highlighted in the peer review), and addresses the concerns of the previous decline application. The Researcher(s) explained personal or offensive questions were removed due to the retrospective data analysis. The new questionnaire has been tested. Some examples are the removal of body size and financial information.
6. The Researcher(s) explained the specialist nurses, who are approaching participants with the questionnaire, are suitable to approach participants. The Researcher(s) clarified that members of the study team conduct study related procedures, so the burden on the health institution is mitigated.
7. The Committee queried whether the peer review comment on study design, in relation to other factors related to variations in outcomes that occur within breast cancer patient populations, such as time of diagnosis, were considered. The Committee also noted that they need to have a statistician review and input into their proposal. The Committee noted that to get representative benefits from the study the researchers need to take these factors into account. The Researcher(s) acknowledged women have broad spectrum of severity of the disease. The Researcher(s) plan to link responses from questionnaire to the histology (stage of diagnosis). This will occur in future, and will address this concern.
8. The Committee asked for an overview of the ethical considerations that had been identified by The Researcher(s). The Researcher(s) explained that the sensitivity of delivering the questionnaire has been managed. They have tested it and had positive feedback (with potential participants).

Summary of ethical issues (outstanding)

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

1. The Researcher(s) explained that the study would include lifestyle information in the current cancer registries, which is an important data point that is currently missing. The researchers explained that they intend to collect and enter their data as new variables in the Auckland Breast Cancer Register (noting that the breast cancer registries are currently being amalgamated into one national register). This could be considered a pilot to test the mechanisms and utility of doing so before considering this as part of the routine data collected nationally for the register, this needs to be reflected in the protocol and in the Participant Information Sheet.
2. The Committee requested that any interventions were removed from the study, as the study aimed to generate a link between lifestyle factors and risk. The Committee noted that it would be too early to say lifestyle factors are problematic until the research is complete and adjusted for all other factors that add to the mortality gap between New Zealand and Australia. The Committee also noted that there is also not evidence to say which interventions might work in this population and what impact they might have on outcomes in order to personalise treatment as claimed. The Committee also queried whether cancer treatment is necessarily a time to address some of these lifestyle issues (eg excess body weight), although it might be for others (eg smoking). The issue of stigma/blame is still potentially problematic in this context.
3. The Committee queried whether any of the lifestyle data was already recorded in clinical notes. The Researcher(s) explained to get the data from clinical notes was very difficult. The Researcher(s) explained to get the data from clinical notes was very difficult. Particularly as there are a lot of missing and unknown data.
4. Please collect data using the New Zealand Census formats for consistency with national data collection. Please refer to the Ethnicity Data Protocols for the Health and Disability Sector, Ministry of Health 2004.
5. The Committee requested that a biostatistician and/or cancer epidemiologist reviews the study protocol, and that their assessment of the required sample size to determine the impact of lifestyle factors be included in the protocol. The Committee noted it would be harmful to conduct research that cannot produce a benefit.
6. Please review the yes/no tick boxes on the consent form and remove any that are not truly optional, and change them to statements.
7. The Committee requested a safety mitigation plan in the protocol due to the potential for questions to result in harms or concerns being raised that require follow up (for example suicidal ideation).
8. Please update the protocol taking into account the suggestions made by the Committee.
9. Please explain whether there are any referral policies for women who are identified as having outstanding issues.

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

1. Remove any treatment or interventions from the information sheet.
2. Include that the information will be stored indefinitely on the Breast Cancer Register (which is consented separately), under its current privacy and confidentiality conditions.

Decision

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

1. The study design must minimise risk of harm. Provide safety protocols for any risks identified due to interaction with participants. (*Ethical Guidelines for Observation Studies* *para 5.5*).
2. Please amend the information sheet and consent form, and assent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Observation Studies* *para 6.11*).
3. Please provide evidence of favourable independent peer review of the study protocol (*Ethical Guidelines for Observational Studies Appendix*).

This following information will be reviewed, and a final decision made on the application, by the full Committee, electronically.

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| **6** | **Ethics ref:** | **15/NTA/199** |
|  | Title: | Starship Hospital wide Investigation of Plasma-Lyte® 148 vs. 0.9% Saline (SHIPS) |
|  | Principal Investigator: | Dr Brent McSharry |
|  | Sponsor: |  |
|  | Clock Start Date: | 19 November 2015 |

Dr Brent McSharry was present in person 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 Researcher(s) explained the scientific context of the study. Early practice used 0.18% sodium fluid, but this was discontinued in the UK in 1993 due to increased SAEs. This hypothesis was confirmed in NSW in 2013 study.
2. Practice then moved to 0.45% sodium (recent studies in adults have compared PlasmaLyte 148 equivalent to 0.9% saline) as standard practice. This increased level is now standard practice.
3. 0.9% saline is currently given to 3% of children presenting to Starship ED.
4. Clinicians at Starship are in agreement that isotonic fluids should be prescribed but are at equipoise as to whether this should be 0.9% saline or PlasmaLyte148. Saline is considerably cheaper.
5. The trial is thus comparing two standard fluids.
6. Children will be randomized to either arm. Children in both arms will received standardised monitoring as per the protocol.
7. This is a hospital wide study.
8. Current practice is varied between New Zealand and Australia, and by clinicians.

Summary of ethical issues (resolved)

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

1. The Researcher(s) explained the glucose premade formula for this study, explaining that currently to have glucose formula they add glucose when required to current formula (same with other additives e.g. potassium). The Researcher(s) explained that this is a risk as human error can result in inaccurate fluids. The study mitigates this risk by providing premixed solution sets, providing a benefit to participants (and all children receiving fluids in the hospital wide study).
2. The Researcher(s) explained Gillick competence would be the measure for children to provide ‘opt out’ consent for themselves.
3. The Researcher(s) explained that any treatment, once the trial is underway, is not managed differently in or outside the trial. Clinician discretion to treat as they want remains unchanged. Data collected is standard care data. If a participant opts out their data will be removed.
4. The Researcher(s) explained that is very difficult to effectively run the study without everyone being enrolled in the whole hospital approach. There are risks due to use of the IV fluid, and good reason to study IV fluids. There is a desire to minimise IV fluid variation among clinicians.
5. (P.4.1) The Researcher(s) explained Maori consultation has been undertaken.
6. The Committee queried the analysis planned. Will this study determine whether one is superior in terms of adverse events (eg neurological or renal effects)? The Researcher(s) explained it depended, though they will not get that endpoint from this study – this is a feasibility study to determine if we can run a large scale study.
7. The Committee noted there is sufficient scientific evidence that sick children need a higher level of sodium (eg children in ED, ICU or theatre).
8. The Researcher(s) explained that the study would be enrolling all children entering Starship. The intention is to make either fluid standard practice, as either would be better than current practice. Either treatment can be offered now at clinician discretion. A trial is however required to demonstrate the hypothesis that 0.9% saline has no difference on average hospital length of stay.

Summary of ethical issues (outstanding)

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

1. The Committee discussed the Hospital wide approach, and the practical difficulties with seeking consent. Please explain the rationale for an opt out consent process more fully. The Researcher(s) explained that if approved all patients receiving fluids throughout the hospital would receive one of the two. The study has a cross over design. The opt out consent relates to use of data, not for treatment.
2. The Committee asked how the researchers would know parents have had opportunity to opt out. The Researcher(s) explained that they don’t think they could feasibly have a consent process (would need to be half patients that go through Starship).
3. The Committee discussed opt out consent and felt that there was not enough of a structured plan to be able to ensure patients had had an opportunity to opt out.
4. The Committee requested a reasoned justification of not using an opt in consent model, noting that opt out required interaction with patients, so why was it not possible to seek consent during that time? The Researcher(s) explained that participants would be continually offered the Participant Information Sheet to opt out, and they would do their best to give people as many opportunities to opt out.
5. The Committee noted there could be a list to cross reference who had been approached about opting out. The Researcher(s) explained that a list would be helpful, but added that it is hard if there is a “one off” fluid given. Fluid will be given by clinician discretion. In some cases it will be hard to be sure who has opted out if this occurred for less than an hour at 4am, for example. The Researcher(s) can track those who have been on fluid long term (longer than few hours) and we have research nurses to approach these potential participants.
6. The Committee requested robust methods to ensure patients have multiple opportunities to opt out of their data being used in the study. Please explain if more publicity of the study can occur around the hospital.
7. The Committee explained that in order to enrol children into the study without their parent’s consent requires the treatment to meet the best interests test of the Health and Disability Commission Code of Rights (Right 7.4). This means that individual participants must benefit from participation.
8. Right 7.4 of the HDC Code of Rights states that “Where a consumer is not competent to make an informed choice and give informed consent, and no person entitled to consent on behalf of the consumer is available, the provider may provide services where –

a) It is in the best interests of the consumer; and

b) Reasonable steps have been taken to ascertain the views of the consumer; and

c) Either, -

i. If the consumer's views have been ascertained, and having regard to those views, the provider believes, on reasonable grounds, that the provision of the services is consistent with the informed choice the consumer would make if he or she were competent; or

ii. If the consumer's views have not been ascertained, the provider takes into account the views of other suitable persons who are interested in the welfare of the consumer and available to advise the provider.”

1. Right 9 ensures that these rights extend to those occasions when a consumer is participating in, or it is proposed that a consumer participate in, teaching or research.
2. It is possible to approve a study (under Right 7.4) if it can be shown that participation is in the best interest of the consumer and they take into account the views of other suitable persons or believe that the consumer would wish to consent if they were able to. In these cases the participant receives treatment, as they would in usual care. Then consent is sought to use the data for research.
3. The Committee noted that there is benefit to participants as there is no need to mix fluids; the hospital delivery will be safer while the study is running, and after once the superior fluid is scientifically backed by evidence.
4. The Committee noted that the researchers should be familiar with the legal context of their research and requested that they seek legal advice, to ensure patients are safe and the law is followed. This is to protect participants and the researchers.
5. The legal requirements are quite clear; participation in the trial must in the best interest of the individual child. Could the researcher please restate the best interest argument bearing in mind the committee needs more than just an assertion that the children will receive best practice monitoring?
6. The Committee requested assent forms for younger children. There is guidance on assent forms at <http://ethics.health.govt.nz/guidance-materials/assent-guidance>

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

1. The Committee asked what data goes overseas (reference to Vanderbilt University data collection mechanism). The Researcher(s) explained that the data is held locally at the University of Auckland. The information is held on servers. The Committee requested information on who can access data is added to confidentiality section of Participant Information Sheet.

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Please provide age appropriate information sheets and assent forms for younger participants and amend the existing information sheets and assent/consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Provide further information on the recruitment process (*Ethical Guidelines for Intervention Studies para 6.2).*
* Provide a justification to enrol participants into the study, by randomising their standard of care, without consent.
* Justify the use of opt out consent, and mitigate any additional risks to participants, over opt in consent. (*Ethical Guidelines for Intervention Studies Appendix 2 – Research Involving Children and Research Involving Unconscious Participants).*
* *Confirm* legal advice has been sought and the researchers are satisfied the study is within the law.

This following information will be reviewed, and a final decision made on the application, by Dr Karen Bartholomew and Dr Brian Fergus.

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| **7** | **Ethics ref:** | **15/NTA/200** |
|  | Title: | TTM-TBI: Feasibility |
|  | Principal Investigator: | Dr Paul Young |
|  | Sponsor: |  |
|  | Clock Start Date: | 19 November 2015 |

Dr Paul Young was present by teleconference 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 Committee thanked the researcher for their cover letter explaining ethical issues involved in the study, and noted the previous legal advice sought.
2. The study investigates current practice guidelines for temperature control with adults who have severe traumatic brain injury in ICU.
3. The two arms of the study are within realm of standard care.
4. One arm reflects an aspirational standard care, or ideal standard of care, and one is a more realistic standard care.
5. One approach is strict control of body temperature that aims to maintain regular temperature of patients. The other approach reflects what happens more commonly which is more a more reactive approach, i.e. waiting for temperature to change then treating.
6. The means to control temperature is the same between both arms.
7. There is equipoise, as there is clinical uncertainty whether it is beneficial to control strictly or not, and both arms involve standard care treatment.
8. This is feasibility study to see if this is possible to control temperate.
9. The protocol is not prescriptive of temperature control - treating clinician retains discretion to treat as necessary.

Summary of ethical issues (resolved)

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

1. The Committee noted best interests was the enrolment method used.
2. The Researcher(s) explained that there is no consent for the treatment, but family views attained where possible, and then consent for use of data. A robust process for doing so was provided by the Researcher(s) and they commented on their experience using this process for a number of ICU studies.
3. The Committee asked about peer review – were there any comments? The Researcher(s) stated yes, and can provide the actual comments and response. Please email to [hdecs@moh.govt.nz](mailto:hdecs@moh.govt.nz)
4. The Researcher(s) explained the additional workshops with ICU research groups. These meetings had 25 experts who discussed protocol.
5. The Researcher(s) explained the further consultation and peer review with clinical community. For example, they had presented also to ICU clinical trials group with over 100 leading experts.

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

1. The Committee requested that tick boxes that are not truly optional were removed from the Participant Information Sheet.

Decision

This application was *approved* by consensus.

## General business

1. The Committee noted the content of the “noting section” of the agenda.
2. The Committee discussed the issue of a researcher tabling laboratory cassettes and slides containing human tissue. Bringing tissue out of the laboratory and placing it on a table with food does raise concerns about awareness on the part of the researcher, in terms of following laboratory protocol. The issue is being addressed by the researcher, as they have been asked to consult with the Maori Research Office. The Chair will also discuss the matter directly with the researcher and the appropriate Maori Review committees.
3. The Committee discussed ethnicity data collection. Members discussed the repetitive issues surrounding the capture of ethnicity in all applications and suggest that all researchers understand why they are collecting ethnicity (i.e., **how** and **why** will it be used in the analysis) and that a correct capture of ethnicity data is performed – e.g. self-reported when possible and conforming to census data collection protocol. The Secretariat noted this was a topic that had been discussed at Chairs day, and will follow up with the Chairpersons and HDEC members on Committee consistency.
4. The Chair reminded the Committee of the date and time of its next scheduled meeting, namely:

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| --- | --- |
| **Meeting date:** | 09 February 2016, 01:00 PM |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

1. **Problem with 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 5pm