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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 16 October 2018 |
| **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 18 September 2018 |
| 1:30pm | New applications (see over for details) |
|  | i 18/NTA/165  ii 18/NTA/166  iii 18/NTA/168  iv 18/NTA/170  v 18/NTA/171  vi 18/NTA/172 **(CLOSED)**  vii 18/NTA/173  viii 18/NTA/174  ix 18/NTA/175  x 18/NTA/176  xi 18/NTA/177  xii 18/NTA/178 |
| 6:30pm | General business:   * Noting section of agenda |
| 6:45pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Brian Fergus | Lay (consumer/community perspectives) | 11/11/2015 | 11/11/2018 | Present |
| Dr Karen Bartholomew | Non-lay (intervention studies) | 13/05/2016 | 13/05/2019 | Present |
| Dr Christine Crooks | Non-lay (intervention studies) | 11/11/2015 | 11/11/2018 | Present |
| Mrs Helen Walker (Co-Opted) | Lay (consumer/community perspectives) | 27/10/2015 | 27/10/2019 | Present |
| Dr Kate Parker | Non-lay (observational studies) | 11/11/2015 | 11/11/2018 | Present |
| Dr Catherine Jackson | Non-lay (health/disability service provision) | 11/11/2016 | 11/11/2019 | Present |
| Ms Toni Millar | Lay (consumer/community perspectives) | 11/11/2016 | 11/11/2019 | Present |
| Dr Cordelia Thomas (Co-Opted) | Lay (The Law) | 20/05/2017 | 20/05/2020 | Present |
| Ms Rochelle Style | Lay (ethical/moral reasoning) | 14/06/2017 | 14/06/2020 | Apologies |

## Welcome

The Chair opened the meeting at 1:00pm and welcomed Committee members, noting that apologies had been received from Ms Rochelle Style.

The Chair noted that it would be necessary to co-opt members of other HDECs in accordance with the Standard Operating Procedures. Mrs Helen Walker and Dr Cordelia Thomas confirmed their eligibility, and were co-opted by the Chair as members of the Committee for the duration of the meeting.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

## Confirmation of previous minutes

The minutes of the meeting of 16 October 2018 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **18/NTA/165** |
|  | Title: | POISE-3 |
|  | Principal Investigator: | Dr Elizabeth Maxwell |
|  | Sponsor: | Auckland District Health Board |
|  | Clock Start Date: | 24 September 2018 |

Dr Elizabeth Maxwell 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 Committee noted its understanding that the Researchers want to do two studies with same outcomes. The main study compares TXA to placebo and then anybody who is in that study who also has hypotension will be randomised to have hypotension avoidance or standard of care.

Summary of ethical issues (resolved)

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

1. The Committee queried whether people can opt out of the second part of the study. The Researchers advised that they can opt out but that it is not encouraged and that they would rather that the patients opt out of the study as they are trying to get as many people as possible recruited into both arms of the study. Current recruitment in two other countries is 84-100% in the second study.
2. The Committee queried whether it is important that patients with hypertension are equally distributed between the TXA and placebo arm. The Committee noted that it could be a risk that quite by chance they end up with more hypertensive in one of the arms. The Researchers noted that because of the size of the trial that is not likely to happen. The large number of patients will mean that there is even distribution.
3. The Committee queried whether people will have a chance to think about being in the study before they consent. There is a branch in the study that does allow for recruitment of acute or emergency surgery and the Researchers have a protocol in place for how they would approach people on the day of surgery. If this wasn’t deemed to be enough time then those patients will be excluded. The Committee noted that it generally likes to see that people are given time to go away and think about whether or not to take part in a study and that there are some people in the New Zealand population that don’t like to say no to people and they might opt out by not turning up for the study. The Researchers are mindful of avoiding coercion and the time pressure and they would exclude these patients if there is not enough time. Most of the patients who will enrol in this study will be coming through the clinic and not triaged on the day and will be seen beforehand and have time to consider participation.
4. The Committee sought clarification that the Researchers will exclude patients who have dementia as the case report form has a post-op question that asks about dementia. The Researchers confirmed that they will only recruit competent people to this study. One of the things for follow up is a holistic disability score and that is probably why this question is being asked.

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

1. The Committee noted that the above points numbered 1 and 2 are not obvious in the Participant Information Sheet and suggested that a diagram or flow chart could be added help make this clear for participants. The part that is specifically for those with hypertension could be phrased differently and state something along the lines of if you don’t have hypertension then you don’t need to read that part of the PIS.
2. The Committee suggested that the Researchers start by saying something along the lines of *We are doing a study to try and answer two questions. The first question is about X and the second question is about X. For both parts of the study the outcomes we want to measure are similar.*
3. At the end of the first paragraph it is stated that there will be enough information to support the safety and effectiveness of using TXA. The Committee noted that this statement presupposes the results of the study and recommended that this statement be removed.
4. The Committee would like to see more information about people who are being managed to avoid hypotension. The Committee noted that the protocol was clear and includes stopping medicines and outlining the process for what will happen. Please make clear what they’re stopping, what will happen if they have a problem and will they go home with the same medicines that they came in on.
5. Because TXA is being used the associated adverse events should be listed. The Committee noted that the Researchers could point out that it is part of standard of care and reactions are rare but they should still be listed as they are important for the patient to know.
6. The Committee noted the statement that if patients withdraw from the study then their study data will be taken out of the study. Normally, what the Committee sees is that data collected up to the point of withdrawal will be kept for scientific validity. The Committee suggested that the Researchers consider this option and if they do then also amend the consent form to reflect this.
7. Accessing medical records is a study activity and as such needs to be stated in both the information sheet and consent forms. Please ensure that this statement is in the consent form and also a statement that participants understand the compensation provision and also the point above about understanding that consent to the Researchers using data up to the point at which they withdraw from the study.
8. Please update the advocacy email to read: advocacy@advocacy.org.nz
9. Please review the documents for jargon language, for example. “off label” which is an American term and reword or remove.
10. Page 2: introduces the term “hypertension” when previously “high blood pressure” has been used. People may not necessarily know that the two are the same. The Committee also noted the statement because you are participating in a randomised controlled trial you will be “required” to sign a consent form. Please replace the work “required” with “asked” to sign consent.
11. Page 2: please specify that participants will be asked to complete a *health* questionnaire.
12. Page 3, under the heading ‘TXA only’ says “only of medication given during your surgery”. Please clarify. Please also revise the content here as some of it refers to procedures and not risks.
13. The Committee queried whether there are risks for people with high blood pressure coming off their meds before surgery. The Researchers stated that evidence shows that the risks are for people who have low blood pressure. Hypertension in a post-operative setting is not a harmful thing. The Committee suggested that the Researchers could state in the risks section that they are not worried about people stopping meds and they don’t expect this to be problematic for this short period of time.
14. The Committee noted that the information in relation to high and low blood pressure could be stated more clearly and simply. They could say the intervention part of this study is that they want to make sure that a person’s blood pressure isn’t too low and that they will give people medicines to bring it up if it is. Please use the terms “high” and “low” blood pressure rather than hypertension and hypotension.
15. The Committee suggested that part of the Researchers’ revision of the participant information sheets and consent forms involves referring to the HDEC template at: <https://ethics.health.govt.nz/> and adopting some of the wording as it is easier to understand.
16. The Committee also suggested that the Researchers ask a lay person to read the document before they submit again to HDEC to check whether they understand and seek their feedback.

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*).

This information will be reviewed, and a final decision made on the application, by Dr Cordelia Thomas and Dr Kate Parker.

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| **2** | **Ethics ref:** | **18/NTA/166** |
|  | Title: | Spinal Cord Stimulation in the treatment of Chronic, Intractable Pain using the Nalu Neurostimulation System |
|  | Principal Investigator: | Professor Alan Merry |
|  | Sponsor: | Nalu Medical |
|  | Clock Start Date: | 27 September 2018 |

Prof Alan Merry 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 asked the Researcher to introduce the study and to highlight how the three different information sheets for three different methods submitted with this application are different as this was not clear in the study protocol.
2. An American company has approached the Researchers in New Zealand with technology that appears to be less invasive than the current standard of care therapy for spinal cord stimulation. In other respects it is similar but the device itself is much smaller than the current one. The study as a whole can be done in a single procedure which is what the Researchers in this study are proposing to do or it can be done as a two procedure study and a third in between (which is the American model). The Researcher again confirmed that although not clear in the application this study in New Zealand will offer participants the single procedure option.

Summary of Ethical Issues

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

1. The Researcher expects that there will be up to five participants in the New Zealand study. The Committee noted that the peer reviewer of this study protocol thought that five participants is a small number and had suggested that a few people be looked at initially and then the Researchers review results. The Researcher noted that this is a difficult study to recruit to as there is a restricted clinical indication i.e. patients with single-sided leg pain with or without back pain but with predominant leg pain. The Researcher noted that if they could recruit those numbers they would do so but practically in New Zealand in the next 12 months this would not likely be possible.
2. In the application the Researcher talks about this study being a feasibility study. The Committee asked whether this is the case and whether it is feasible to study this device. The Researcher noted it is a recruitment rather than a comparative study and in this regard it is a feasibility study. The feasibility will be studied by collecting standard outcomes about this device to show whether it is acceptable to people. The Committee asked that this be explained more and clearly to people in the information sheet and that it is the first time that this device is being studied in humans. The technology is the same but the physical device is not. The big difference is that patients will wear an external device rather than have an implant.
3. The Committee noted that some of the questionnaires have names on them and in the interests of protecting the confidentially of participants the Committee asked that names be removed and replaced with a unique study ID code.
4. The Committee sought clarification on how the safety of the device will be monitored. In the application is it stated that an independent medical person will meet with the sponsor once a year. The Researcher acknowledged that this may not appear to be adequate safety monitoring from the Committee’s point of view. The patients will be clinic patients and their safety will be paramount as it always is.
5. The Committee asked for clarification about whether the device will stay in permanently once implanted. The Researcher confirmed that it would because the external part can be recharged. In the longer term the patients need to be maintained and have ongoing care and there is the need to ensure that they will be in circumstances such as the company going out of business. The Researcher advised that he had had discussion with ACC about funding ongoing use of the device in such an event and the Committee noted its confusion that ACC would fund ongoing use of a device in a sponsored study.
6. The Committee noted that it deals with ACC in the context of compensation for injury and when in a sponsored trial people are not eligible to make a claim for ACC compensation and the sponsor is expected to have insurance in place to cover compensation to ACC equivalent standard. In terms of cost for the device the Committee’s expectation is that the sponsor pays for the cost of the device not ACC.

The Committee requested the following changes be made to the participant information sheet and consent forms:

1. The Committee thanked the Researcher for providing clarification on the study design and noted that given that three information sheets had been submitted with this application that it was not clear which of these it should be considering as part of this New Zealand study. They all look very similar and don’t clarify which method is being used.
2. The Committee noted certain aspects were unclear including how much time there is between visits. The Committee suggested stating in months rather than days would be clearer. The Committee suggested a graphic contained on page 24 of the protocol would be a helpful inclusion in this regard.
3. The Committee suggested that a diagram or photo of the device to show comparison with what is currently used be included.
4. The Committee noted that sponsors can’t suppress the results which is what the PIS states on page 9. Please remove this statement One PIS has Australian references including reference to the TGA but does not note that we do not have a device regulator in New Zealand. The other two information sheets have been updated. Please ensure that the PIS to be used for this study is resubmitted with updated New Zealand references.
5. Please clarify the number of stated participants differs across the application and in the participant information sheet and this needs to be clarified. Please clarify and make sure that this is consistent in the application and in the information sheet.
6. The Committee noted that information in the PIS should also match statements given in the consent form. Please revise both documents and amend as required.
7. In one part of the information sheet it is stated that participants will be contacted by Nalu Medical to assess how the device is working. The fact that personal information will be given to Nalu Medical is not currently stated in the information sheet. The Committee noted that personal details should not be given to the sponsor and acknowledged that this would alter the study design. Please remove this statement from the information sheet.

Decision

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

* The Committee is supportive of the application, would like to see the work done in New Zealand and would welcome a new application. That is, with one procedure and with one participant information sheet that has been revised, amended and has clearer information for the participants.
* 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*).

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| **3** | **Ethics ref:** | **18/NTA/168** |
|  | Title: | ICON 9 |
|  | Principal Investigator: | Dr Michelle Vaughan |
|  | Sponsor: |  |
|  | Clock Start Date: | 04 October 2018 |

No member of the research team was present 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 ethical issues (outstanding)

The main ethical issues considered by the Committee and that require addressing by the Researcher were as follows.

1. The Committee noted that this is a phase III study and queried why it is investigator led as it appears that Astra Zeneca could stand to benefit financially from this study and the question of how is this study not sponsored was raised. The Committee noted that Astra Zeneca will receive both samples and data and the application states that the data will be potentially identifiable. Astra Zeneca appears to have rights to change the publications. The Committee agreed that those points meet sponsor criteria. However it would seek clarification from the Researchers in relation to this.
2. The Committee would like to see justification for why the sponsors will receive potentially identifiable data.
3. The Committee noted that the FUR information makes reference to this aspect being “extended research”. Future unspecified research is not extended research. Mandatory extended research as part of the study is okay to use but the rest of it is not extended research. In the FUR information it is not clear whether left-over samples or extra samples will be used and this is not clear in the protocol either. Mandatory biomarker testing is also not clearly specified in the study protocol. Please provide clarification for the Committee and specify in the protocol also.
4. Section a.1.6 of the application form states that there are no ethical concerns. The Committee noted that important ethical considerations that could have been outlined here include tissue being sent overseas and also the use of tissue in future unspecified research.
5. Section r.5.4 in the application form: the Committee queried the co-ordinating physician also being the oncology physician and would like to know how the Researchers intend to manage this conflict of interest.
6. The Committee noted that evidence of insurance submitted with this application shows an expiry date of 31 August. Please ensure that insurance is up to date.

The Committee requested the following changes be made to the participant information sheet and consent forms:

Main Information Sheet and Consent Form

1. The Committee noted the statement that one of the trial drugs is not approved in Australia and New Zealand. Please amend to reflect that it is not approved anywhere in world.
2. Please provide more information about the frequency and side-effects of the two study drugs. The Committee suggested that information in relation to this be included in one place in a table format so that it is clear for participants.
3. Please separate out the references to future unspecified research and place that information in the optional information sheet for future unspecified research. In the separate FUR sheet in relation to tissue that will be sent overseas please be specific about where it will be sent and state the location/s. In other words please state who the other collaborators are.
4. In relation to mandatory BRACA testing please be clear that this is confirmation for entry into the study and why.
5. Please clarify for the Committee and confirm whether it is correct that they have available genetic and family counselling as it is the Committee’s understanding that the current genetic counselling services do not do this for research in NZ.
6. Astra Zeneca’s involvement in the trial is first mentioned on page 30. This is too late in the document and should be stated up front.
7. The information on page 3 of the document appears to be a repeat of the information stated on page 1. Please revise and remove repetition.
8. The section about the purpose of the study is overly technical and as such not lay person friendly. Please rewrite in lay language.
9. Page 2 talks about how long the study will be run for and states that participants will keep taking medication until the disease is no longer responding to treatment or possibly beyond if benefiting from treatment. The committee noted that a participant can’t be both benefiting and not benefiting at the same time and asked that this statement be revised and reworded in a way that is clearer and makes more sense.
10. Page 5: the Committee noted that the number of visits required for this study are significantly more than standard of care and that participants should therefore be reimbursed for their travel and parking. Please state that the number of visits are increased and please consider reimbursing participants for this.
11. Page 6 mentions study costs in Australia. Please revise this and make it relevant for New Zealand participants.
12. Page 7, section 7 mentions having a longer cancer-free time and there is no evidence of this. Please justify this statement or remove it from the document.
13. Page 9 states that “Both tablets may affect your ability to drive or use machines. If you feel dizzy, weak or tired taking this treatment you should take special care when driving or using tools.” If it is risky to drive, please be specific about this and state whether they should refrain from driving.
14. Page 10: please remove reference to future unspecified research and include this information in the separate FUR consent form.
15. Page 11. The Committee noted that the study number contains birth date and initials. Please make this a unique study number that does not contain birth date and initials. Please also make clear that participants can legally withdraw verbally from the study without the need to fill in a withdraw form.
16. Page 12. The Committee noted that the sponsor cannot stop the study for commercial reasons. Please remove this statement.
17. Page 12, section 13 under ‘does the sponsor intend to make the study drug available after the study?’ The Committee asked that the researchers confirm that Astra Zeneca isn’t involved as a sponsor. The Committee understands from the application form that the drugs are being donated but at the same time it has been stated that Astra Zeneca has rights over publication.
18. The Committee noted that more statements are needed in the consent form about what participants are consenting to and suggested that the Researchers refer to the HDEC pro forma for guidance about what to include: <https://ethics.health.govt.nz/guides-templates-forms-0/participant-information-sheet-templates>
19. Please clarify what will happen at the end of 6 years if patients are still in the study and make this clear in the participant information sheet. For example, will they still be able to have access to and take the drug.
20. Please state that some of the questions from the study questionnaires are of a personal nature and also please outline the process for what will happen if a participant is found to be depressed.
21. Please clarify for the Committee why you do not intend to collect ethnicity data.
22. The consent form asks participants to consent to their GP being advised of their being in the study but this is not set out in the information sheet for participants. Please advise participants of this intention in the PIS.
23. Please clarify for the Committee and confirm whether it is correct that they have available genetic and family counselling as it is the Committee’s understanding that the current genetic counselling services do not do this for research in NZ.
24. Please include HDEC contact details.
25. Please update the advocacy email to read: advocacy@advocacy.org.nz

Optional Extended Research Participant Information Sheet and Consent Form

1. The optional extended research information sheet talks about future related research studies related to *this* cancer and then on the declaration by participant states related to *general* cancer research. This is contradictory. Please clarify for the Committee and please also be clear in the information sheets about which it is.

Decision

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

* 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 amend the protocol to specify whether mandatory biomarker testing will be done, whether left over samples or extra samples will be used in any future unspecified research. (*Ethical Guidelines for Intervention Studies* *para 5.4)*
* Please advise how you intend to manage the conflict of interest that arises from the CI also being a participant’s oncology physician. (*Ethical Guidelines for Intervention Studies* *para 6.3)*
* Please provide clarification about who the study sponsor is and whether Astra Zeneca is in fact the study sponsor. (*Ethical Guidelines for Intervention Studies* *para 8.4)*

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| **4** | **Ethics ref:** | **18/NTA/170** |
|  | Title: | Neurodevelopmental outcomes in preschool children following enteroviral and parechoviral meningitis |
|  | Principal Investigator: | Dr Natalie Martin |
|  | Sponsor: |  |
|  | Clock Start Date: | 04 October 2018 |

Dr Natalie Martin 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 Researcher explained that a lot is known about the outcomes from bacterial meningitis, like seizures, hearing problems and developmental problems but nowadays most meningitis is caused by viruses partly because of the effectiveness of vaccine programmes in countries like New Zealand.
2. This study will look at whether there are ongoing developmental sequelae or things like hearing problems for children who have had viral meningitis.
3. To do this the Researchers will do some in-depth play based developmental assessments in children who have had viral meningitis.
4. The assessment is the Bayley Scale which has been used in many studies including in New Zealand. These assessments will be done by a psychologist. Additionally there are some brief questions for parents asked beforehand such as questions about concerns about hearing or other medical problems. Any concerns will be followed up with the parents’ consent.

Summary of ethical issues (resolved)

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

1. The Researcher confirmed for the Committee that a participant information sheet and consent form and a separate letter that invites families to take part in the study were submitted with this application.
2. The Committee queried how the Researchers intend to initially contact potential participants. The Researcher explained that they do not routinely follow children who have viral meningitis and they don’t normally see them in clinic so the way they will identify them is by searching Canterbury Health Laboratory’s records to check for children who have had enterovirus of parachovirus and then sending families the letter to ask if they are interested in taking part in the study. The Researcher noted that families will be interested in having a free developmental assessment that gives them information about their child.
3. The families will know that their child has been in hospital with meningitis and the letter is careful and states that most children or babies who had viral meningitis recover completely. Then it says that there are a few small studies that found that some might have some mild difficulties and so more needs to be known about children’s health and development and then explains what the study is about.
4. The Committee noted that the letter may have confidential information in it and queried how confident the Researchers are that it will be sent to current addresses that aren’t confirmed and without prior consent. The Committee agreed that this is technically unconsented data but it is the only way that the Researchers will potentially get enrolment in the study and it is optional and parents don’t have to respond. In relation the wording in the letter as it stands the Committee was satisfied that the wording is such that it does not disclose information that would pose a serious breach of confidentiality.
5. Section f.1.2 in the application form. The Committee asked whether there were any other specifics in relation to Pacific Islanders and other populations such as Asian New Zealanders. The Researcher noted that enterovirus infections incidence is higher in Asian populations. This is not genetic as opposed to geography but it is not yet known whether there are differences in rates of viral meningitis in children of different ethnicities. Ethnicity data will be collected in this study and the Researcher noted that this will not be a big study and it won’t be likely that they can answer the question about ethnicity. They may be able to think about this in future in relation to national coded data.
6. In relation to sample size the Committee queried whether there are adequate numbers in this study for the study’s secondary outcome which is looking at whether they have white cells in their CSF. The Committee asked the Researchers whether they think there are enough people in each group to see a difference. The Committee noted that the numbers start to get small and wondered whether a multi-centre study with other researchers might give better population representativeness. The Researcher agreed that the numbers are small and that they might become descriptive in this particular study in terms of what the scores are. This study has been funded by an Otago University Research grant and a bigger study is not possible at the moment. If findings of this study are significant the Researchers could look to do bigger studies or to combine their data with international studies or other centres in New Zealand which Maori and Pacific populations to give information about our indigenous population.

Summary of ethical issues (outstanding)

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

1. The Committee noted the study protocol is briefer than it would normally see and noted that the Researcher was asking about medication and vaccination history as asked the Researcher to explain how this is relevant to the study outcome measures. The Committee asked the Researcher to consider how important this clinical information is and if it is an important outcome suggested that it be collected by the NIR. If it is not relevant to the outcome the Committee suggested that the Researcher remove the request to collect it. The Committee noted the importance of only collecting information that is of relevance for the outcome and noted that vaccine for this condition is not currently available in New Zealand.
2. The Committee noted it did not see any information in the study protocol about ensuring safety of staff at home visits. The Committee asked the Researcher to give some thought about how this will be managed should staff encounter a problem at the home visits and what the expectations would be. The Committee noted that the hospital will have a visiting protocol and the Researcher could refer to that for guidance. The Committee would like to see that there has been some thought given to this and a plan set out in the study protocol
3. The Committee requested that the Researcher include a management plan in the protocol for what will happen in the event a child or parent becomes distressed during the assessment
4. The Committee queried how likely it is that some abnormal findings will be identified that are unknown or unexpected for the parent. The Researcher noted that this is unlikely. However given it is possible the Committee would like to see a plan in the protocol for what will happen in the event that abnormal findings are identified.
5. The Bayley Scale Assessment, which was not submitted with the original application involves play and some play based questions all with the child. The Committee asked the Researcher to confirm whether there are questions for the parent and to provide the Committee with a copy if there are.
6. The Committee requested the following changes be made to the participant information sheet and consent forms.
7. Please include Maori support number in PIS
8. The Committee queried whether the Researchers plan to exclude children who have pre-existing developmental diagnoses. The Researcher advised that they are not going to exclude them but they will record them and provision for this is in the questionnaire. The Committee noted that the questionnaire is a study activity and asked the Researcher to include this information under ‘What does the study involve?’ in the participant information sheet. Please also include information about the types of questions that will be asked and how long it will take to complete.
9. The Committee requested that the Researcher include a management plan in the protocol for what will happen in the event a child or parent becomes distressed during the assessment. The Committee also requested that something along the lines of “if your child or you become distressed at any time during the assessment we can stop the assessment” also be included in the information sheet.
10. The Committee queried how likely it is that some abnormal findings will be identified that are unknown or unexpected for the parent. The Researcher noted that this is unlikely. However given it is possible the Committee would like to see a plan in the protocol for what will happen in the event that abnormal findings are identified. Please also note in the participant information sheet that if there are any findings that the Researchers will discuss them with the parents (and the GP with parents’ permission), and refer to appropriate services.
11. Please state that you will be accessing medical records and including hearing records as this is an activity that is part of this study and as such the participants need to consent to this.
12. Under the heading ‘What is the benefit from being in this study?’: the Committee suggested that it is likely there will be no benefit and asked that the Researchers include a statement along the lines of “Your child may derive no benefit from being in the study” and then state “However, we are hoping it will improve treatment for other children in the future”.
13. Please state that participants will be reimbursed for reasonable travel and parking costs.
14. The Committee sought clarification about whether parents and guardians will be participants in this study or whether they are just providing information. The reference at the top of page 2 of the information sheet suggests that they are. The Researcher advised that this may have been in error as a template has been used. The Committee noted that it has its own template that can be found on the HDEC website and noted that this is a helpful template for Researchers to use in the New Zealand context. Information not included in the information sheet submitted that is in the HDEC template includes information about compensation in the event of injury as a result of being in the study. Although the risk is low in this study it still needs to be shown that the Researchers have considered this.
15. The Committee asked that footers with more information including version number and page numbers be included.
16. Please remove reference to the Multi region ethics committee as this is no longer accurate.
17. Please update with reference to the Northern A Health and Disability Ethics Committee.
18. The Committee noted that in studies involving children information needs to be kept for 10 years from the time they turn 16. In the participant information sheet when revising please include a section on patient rights that includes information that they have the right to withdraw from the study at any time, a right to receive a summary of results (they don’t have to ask for these), a right to see and correct their data, and the right to know where their data will be held and how it will be stored to protect their privacy.
19. Please revise the Consent form so that it talks about “your child” rather than “you”. Please also include the statement that they consent to access of their health records as part of this study.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Observational Studies, para 6.11*)
* Please update the study protocol to include more detail on study procedures. (*Ethical Guidelines of Observational Studies, para 5.5*)

This information will be reviewed, and a final decision made on the application, by Mrs Helen Walker and Dr Catherine Jackson.

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| **5** | **Ethics ref:** | **18/NTA/171** |
|  | Title: | Freestyle Libre alternative site study |
|  | Principal Investigator: | Mr Lindsay McTavish |
|  | Sponsor: |  |
|  | Clock Start Date: | 04 October 2018 |

Mr Lindsay McTavish 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 monitors in this study are currently in use in New Zealand and the site on the back of the arm has been advocated for by the international group, Abbott Pharmaceuticals. Results are validated for that particular clinical application for that position.
2. This study is being done as this site is an unusual place for the wearer and there is anecdotal evidence that users in NZ are placing the device in more accessible positions. This investigator initiated research would investigate the suitability of alternatives to this site. In New Zealand one of the sites patients are using is the top of the buttock but there is no critical evidence to say whether it is accurate or near accurate.
3. Two published papers looking at upper thigh and abdomen as sites show that between the abdomen and back of the arm there is a 40% difference in results and clinically people are being advised not to use alternate sites. This study will look at the upper chest and buttock sites to see whether results are comparable to the back of the arm and also compare results with finger prick and venous samples.
4. Many patients use this device currently in an off licence way and they adjust their insulin on it and poor site placement can lead to hypoglycaemia.

Summary of ethical issues (resolved)

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

1. The Committee sought clarification in relation to the monitor and asked whether it gives continuous feedback on glucose levels or whether it has to be downloaded to get feedback. The Researcher explained that it is designed as a flash glucose sensor. It gives continuous feedback using a handheld sensor and through Bluetooth function data for past eight hours is transferred. What has crept into the clinical setting now are small adaptors that can be put on the sensor and that transfer the information continuously to a cell phone so it is termed as continuous feedback.
2. The Committee asked how big the implant is and whether it needs to be replaced every couple of weeks. It is a filiament of about 6 mm in length and when inserted into the body is fired under the skin by the person themselves. The sensor itself is the size of an old fifty cent coin and is adhered to the skin. For the purpose of this study and to remove bias the Researchers will have their medical students put the monitors on and also remove them. It will stay on 14 days.
3. The device can be made available to participants after the study has finished. The device will be funded by a grant from the Wellington Medical Research foundation pending confirmation.

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 its understanding of the study procedures – that there are three periods in the study. The first period is a two week period on the arm site, the second period is also two weeks but this time on the ABC sites and the third period will involve overnight use with meals and exercise. The Researcher clarified that the first period will be using the normal sensor for two weeks for baseline, then comparator sites and the meals and exercise part is the third component of the second period. This will happen the day after they have the second sensor in in the second period or ABC sites. They won’t stay overnight but will come in early in the morning and leave later that day (10 hours in total). The Committee noted that itis not clear either in the protocol or in the information sheet where the exercise will be done, how it will be supervised and monitored in the case of a medical event and asked that the Researcher make this information clearer in both the protocol and the participant information sheet. Please also state where the research centre mentioned in the protocol is. A flow chart or table would be a helpful way of showing this to potential participants.
2. The Committee did not have time to raise the following with the Researcher at the meeting. However, the Committee noted following discussion with the Researcher that at question p.3.1 in the application form a provisional survey had already been conducted prior to commencing the study and asked that in any response to the Committee the Researcher explain what that survey was about and how it will ensure patients can give informed consent free from undue influence.

The Committee requested the following changes be made to the participant information sheet and consent forms:

1. Please review the document to check for typos and grammar.
2. Please state what will happen to the blood collected for this study, where it will be tested, where it will be stored and for how long and how it will be disposed of.
3. The Committee noted that the application refers to medical students inserting the device. Right 9 of the Code of Patient Rights provides that people must know that they training students will perform certain tasks. Please include in the PIS that students will be doing these tasks. In the interests of consistency, the Committee noted that it would prefer if the lead investigator inserted all of the devices and the Researcher agreed that he would insert and remove all of the devices and that this would be possible as there will be just 20 people in the study.
4. Please state that participants will have their parking expenses reimbursed.
5. The Committee asked that more information about the data and how this will be managed to protect patient rights and confidentiality is needed. If data is to be stored for

future use, please clarify.

Please provide provision for the lead investigator to sign the information sheet.

The Committee recommended that the Researcher refer to the HDEC PIS and Consent form pro-forma that is on the HDEC website: <https://ethics.health.govt.nz/> Please make sure that you use the ACC statement from this document.

1. Please update the advocacy email to read: advocacy@advocacy.org.nz
2. Please update the HDEC Committee to Northern A HDEC
3. Please provide Maori contact person details.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies, para 6.22*)
* Please update the study protocol to include more detail on study procedures. (*Ethical Guidelines of Intervention Studies, para 5.5*)

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

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| **6** | **Ethics ref:** | **18/NTA/172** (**CLOSED**) |
|  | Title: | Neonatal Bubble CPAP Comparison Study |
|  | Principal Investigator: | Mr Jonathan Barrett |
|  | Sponsor: | Fisher & Paykel Healthcare Ltd. |
|  | Clock Start Date: | 04 October 2018 |

Mr Jonathan Barrett 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.

Decision

This application was *provisionally approved* by consensus.

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| **7** | **Ethics ref:** | **18/NTA/173** |
|  | Title: | The CHEWY Trial |
|  | Principal Investigator: | Dr Robyn Billing |
|  | Sponsor: |  |
|  | Clock Start Date: | 04 October 2018 |

Dr Robyn Billing 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 ethical issues (resolved)

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

1. The Committee noted its understanding that the Researchers intend to include 12 – 16 year olds in this study. The Researchers advised that this will not be the case as most participants will be aged 16 and above. The protocol included with this application is for Australia and New Zealand and New Zealand is not planning recruiting participants who are younger than 16 years of age. The Committee noted for future reference that it would be helpful to see this kind of distinction highlighted in a cover letter.
2. The Committee sought justification for why this study will only include women. The Researchers explained that this is because being a woman in and of itself is a risk factor for nausea and vomiting post-surgery.
3. The Researchers intend to recruit elective patients and will be looking at elective patient lists for the week and then calling them that week to see if they are interested in taking part. They will have some time to think about this before agreeing.
4. The Committee queried who will make the initial approach to patients to enrol them. The Researchers will do this and they confirmed that they are not providing any treatment to the participants prior as clinicians.
5. Section p.4.1 on page 20 of the application form. The Committee queried whether there are any known incidence rates for Maori about having nausea post-surgery. There is no known data currently available but they may find out more doing this study.

The committee requested the following changes be made to the participant information sheet and consent forms:

1. Page 2: please amend to give clearer wording about what will happen in relation to how patients will be randomised to the study and why. The statement is made that there will be no change in the standard of care that people will receive but then goes on to say that people will be randomised into two groups.
2. The Committee noted the statement that the patient and the recovery room nurse will know which they are doing but the person observing won’t know. The Researchers explained that the observer will leave the room for 15 minutes at the point that the patient is randomised to the study after it is known that they are feeling nauseous/sick. Before the observer returns the patient will discard the gum. Please make this clearer in the information sheet.
3. Mention of “24 hours later” is made throughout the document and the Committee asked what this is in relation to. The Researchers advised that this is 24 hours from when they reach PACU. Please make this clearer in the information sheet.
4. Under the heading ‘Risks and Disadvantages of Taking Part’ it is stated that “the risks are the same as faced by any patient receiving general anaesthetic.” The Committee queried whether this is the case as the risks are that if patients just get chewing gum then they may continue to feel nauseous. The Risks from THIS research are having either the medication or this chewing gum not from the general anaesthetic as participants are going to have one anyway. Please state that the risks are that the gum may not work and they may need to take medication that they would take normally. The Researchers noted that the risks are the same in both arms as there is always escalation of care. The Committee asked that the Researchers explain this in the information sheet. The risks involved in being part of the research are that it may not be successful and they may be escalated to other treatment and that they will get immediate treatment. The Committee suggested that although the risk of choking on chewing gum is theoretical that it could be added to the information sheet.
5. Page 3: notes that participants’ GPs will be sent a letter. Please add the words “if you agree”.
6. By signing the consent form participants are agreeing to the researchers continuing to review their medical notes and the Committee queried how long this will be for. The Researchers confirmed that this will be until the end of the project. Please make this clear.
7. On the declaration by participant it is stated that participants can withdraw at any time and the Committee noted that usually there is provision for withdrawal of data up to a certain point before it becomes impractical to do so. E.g once it is analysed. Please also change “I may not be randomised” if I don’t have nausea or vomiting to “I will not be randomised”.
8. The information sheet notes that the Researchers will access participant health records as part of this study. Please also include a statement in the consent form that states participants agreed to the Researchers doing this.
9. The questionnaires in this study are quality of life surveys in perioperative medicine field looking at experiences of people having a general anaesthetic rather than being nausea specific. But within there is the impact of nausea and vomiting on that. They compare before and after results of the survey.
10. In the Confidentiality section the Committee suggested that the second paragraph be moved up one as from a patient perspective it can make more sense to say you will code the data, then de-identify it and then share it.
11. Please include the following standard statement in your compensation section: “*If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.”*

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies, para 6.22*)

This information will be reviewed, and a final decision made on the application, by Dr Cordelia Thomas and Dr Catherine Jackson.

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| **8** | **Ethics ref:** | **18/NTA/174** |
|  | Title: | Glucose in Well Babies and their later Neurodevelopment (GLOWiNg) |
|  | Principal Investigator: | Dr Deborah Harris |
|  | Sponsor: |  |
|  | Clock Start Date: | 04 October 2018 |

Dr Deborah Harris and Ms Alana Cumberpatch 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. This researchers have previously done a study, Glucose in Well Babies, or GLOW study, which sought to determine normal glucose and lactate in healthy babies for the first five days after birth. Detailed feeding data was collected to determine what is normal. Previous research has been done in babies with low glucose levels but no research had been done in a cohort of babies to gain evidence on what was normal.
2. The researchers explained that the GLOW babies are a unique cohort of babies – they are all healthy as are their parents. Some of these babies have low blood glucose levels and what the researchers would like to do in this study is follow up on to determine whether or not they have normal neurodevelopmental outcomes.
3. Two phases are planned for this follow up study. Phase 1 which is before the Committee today is a follow up of the babies now that they are three years old. The researchers would like to ask parents to complete two questionnaires. The Ages and Stages questionnaire which is a standard paediatric screening tool looking at communication, movement and socialisation and the other is a home and family questionnaire that collects data about the child’s background and health and also some information about participating in the GLOW study as babies.

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 questionnaires ask for contact details for the child’s grandparents and asked whether collecting this information (without their prior consent) is necessary for this study. The Researchers explained that they ask for the grandparent details because they have found with the results of previous studies that the New Zealand population is mobile and that having grandparent details has helped them contact some parents at a later stage. The Researchers also noted that learnings from the GLOW study were that the extended family “walked in partnership” with the families in the study and that grandparents were a big part of that.
2. The answer at question r.1.1 on page 13 of the application form states that if the Researchers are unable to trace the families that they will initially contact their alternative addresses and if necessary contact their primary health care provider. The Committee asked why the Researchers would contact their primary health care provider. The Researchers explained that when they did the GLOW study they asked participants if they could contact them after completion of the study and that contacting the primary health care provider would be done to help follow up. The Committee explained that the Health Information Privacy Code doesn’t allow for the provider to release patient details without their prior consent. The Researchers explained that when they enrolled participants to the study they informed participants that they might contact them to do the follow up study but they didn’t get consent for the GP to contact them.

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 asked the Researchers what process they have in place in the event that people disclose that any scars have been as a result of abuse. The Researchers noted that they would talk to the family, the steering committee paediatricians and that they would follow guidelines on how to proceed. Paramount would be to keep the child and the person who disclosed the information safe. The Researchers do this as part of their professional lives and reassured the Committee that they would keep the discloser and the child safe and that they would refer to services where appropriate. The Committee asked that they include information about this process as an additional section in the study protocol.

The Committee requested the following changes be made to the participant information sheet and consent forms:

1. The Committee noted that the information sheet is set out in brochure format and accepted that this is suitable for this study but raised the fact that there is no standard information for participants about data management and confidentiality rights. The committee asked that the researchers include statements about how they will manage the study data, keep it confidential and that participants have the right to see information, correct it if it is wrong and withdraw their information from the study. Standard wording on these rights are included in the HDEC pro forma participant information sheet but the Committee noted that the wording is there as a guide and that the Researchers could refer to it and shorten it to fit in their document.
2. The Committee queried the need for the inclusion of a compensation statement in the brochure noting that there is very little risk involved in this study and it agreed that the current statement could be removed from the document.
3. The Committee noted that the family questionnaire includes provision (in the top box) for the inclusion of identifiable information and asked that this be removed and that a study number only be included. The Committee asked that the Researchers also review the document for typos.
4. The Committee asked whether the Researchers intend to keep the data from this study for future use and research. If yes, could the researchers mention this in the section about confidentiality in the information brochure. The Researcher noted that in the protocol they have stated that they intend to follow up again when the children are 4.5 years old. Depending on what they find in this phase 1 at 3 years to interview, do developmental testing and an examination by a paediatrician and vision and hearing. They will be building on this data and continuing to use. The Committee asked that the Researchers include this information in their brochure.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Observational Studies, para 6.10*)
* Please update the study protocol to include more detail on study procedures. (*Ethical Guidelines of Observational Studies, para 5.5*)

This information will be reviewed, and a final decision made on the application, by Mrs Helen Walker and Dr Karen Bartholomew.

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| **9** | **Ethics ref:** | **18/NTA/175** |
|  | Title: | A Phase 1 Study of ABI-H2158 in Healthy Volunteers |
|  | Principal Investigator: | Professor Ed Gane |
|  | Sponsor: | Clinical Network Services (CNS) Pty Ltd |
|  | Clock Start Date: | 04 October 2018 |

Prof Gane 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.

Dr Catherine Jackson and Dr Christine Crooks declared potential conflicts of interest, and the Committee decided that they could remain in the room but not take part in the discussion or decision making for this application.

Summary of study

1. This study has an umbrella protocol and will be done in three parts. Part one, is a single dose, part two is multiple doses and part three will include patients with chronic hepatitis b. This class of drug is well in development and is a second generation core inhibitor. This study will determine best dose. The first two parts are in healthy volunteers and then moving into patients. 10 different centres are involved in the patient part of this study.
2. The Committee sought clarification on whether the Researchers are involving the patients with Hepatitis B because a third participant information sheet has not been submitted with this application. The Researcher explained that this hasn’t been finalised yet. The third part is scheduled to take place in May or June of next year. The Researchers intend to submit part three prior to starting all patient screening activities.
3. With this in mind the Committee agreed that it would only consider and decide on parts one and two at this meeting. When this is finished and a progress report submitted that includes safety and dose information and approved only then will the Committee look at considering part three.
4. The Committee complemented the Researchers on the answers provided in response to the application’s cultural questions.

The Committee requested the following changes be made to the participant information sheets and consent forms:

1. Page 2, second paragraph under 1.3 randomly has some information about blood sampling under ‘funding’. This is also included under section 6 on page 13 about what goes where. This is slightly confusing.
2. Page 4: please put the information about a different cohort in section 2.2. If information about the different cohorts could be put in a table here this could make things clearer for participants.
3. Page 12: reference to IECs may be an Americanism. Please revise and reword.
4. Page 13: please provide details for the USA lab where the samples will be sent to.

Optional PG study

1. The Committee understands the optional pharmacogenomics for chronic Hep B patients in part three as all of the text refers to understanding Hep B, problems related to Hep B, drug markers in Hep B response and side effects etc. but this study refers only to healthy volunteers. Is there justification for doing optional pharmacogenomics testing in healthy volunteers. The Researcher noted that there doesn’t appear to be a rationale for this. If it was blanket consent for anything then that would make sense but if the Researchers are specifically looking at specific things in this PIS then it is hard to justify. The Researchers will go back to the sponsor and discuss whether that should be removed. The Committee felt that this could be included in part three.

Forms for pregnant partner and consent to be signed once a baby is born

1. The Pregnant Partner form to be signed when it is confirmed that the partner is pregnant should not include reference to the health of the child as parents can only consent to this after the child is born. Please place this in the consent form to be signed once the baby is born.

Decision

This application was *approved* by consensus.

Non Standard Conditions

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies, para 6.22*)

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| **10** | **Ethics ref:** | **18/NTA/176** |
|  | Title: | Is a dementia prevalence study feasible in New Zealand? |
|  | Principal Investigator: | DR SARAH CULLUM |
|  | Sponsor: | University of Auckland |
|  | Clock Start Date: | 04 October 2018 |

Dr Sarah Cullum was present by teleconference and Prof Ngaire Kerse and Dr Margaret Dudley 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 ethical issues (resolved)

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

1. The Committee thanked the Researchers for their application and noted that it is familiar with the dementia prevalence concept and appreciate the need to test out some of the important cultural and feasibility aspects.
2. The Committee raised the issue of the particular cohort of people who aren’t able to consent for themselves. The Committee noted that in New Zealand next-of-kin or proxy consent for another person to take part in research is not legal.
3. The Committee noted that in the cohort of people who aren’t able to consent for themselves it needs to apply the test stated in Right 7(4) of the Health and Disability Code of Patient Rights and that the Researchers need to be able to provide an argument that taking part in the study is in the *best interests* of the participant.
4. The Researchers noted that a case is made in section r.8.1 of the application form that social engagement, opportunity for caregivers to voice their concerns is better for people who don’t know they have dementia to be in contact with the available services and that would happen as part of this. The Committee noted that some justifications have been made but there is no discussion in the papers submitted that Right 7(4) has been met and the Committee needs to know that the Researchers understand that this is the critical issue and that what is being justified is the range of things that need to be done to meet Right 7(4).
5. The Researchers argued that being in this study is in the best interests of people in the sense that they want to benefit their own communities and also they get to have a conversation with a health services professional and in their own language and culture.
6. The Committee noted that *best interests* has to be an individual assessment related to the consumer rather than benefiting the community. It is about whether this individual will be better off for being in the research than they would be if they were not. The second thing to establish is that reasonable steps have been taken to ascertain the consumer’s views and if this is not possible that other suitable persons are consulted. The other people are being consulted only and it is the provider who makes the decision on whether to enrol the person or not. With this in mind the information and consent forms for proxy consent submitted with the papers for this application are contrary to the law.
7. In situations where there is an *activated* enduring power of attorney then they could give consent on behalf of the person as long as it is not a medical experiment. This study does not involve a medical experiment. Section 18 of the PPPR Act provides that an enduring power of attorney or welfare guardian cannot give consent to a medical experiment unless it is to save the person’s life or prevent serious damage to their health.
8. 8The Committee noted that the protocol sets out five points around benefit: assessment, isolation and whether research gives people an opportunity to connect with others, multicultural approach around giving voice to the carer around carer needs and then participants’ non-English speaking ethnic groups (access). The Committee accepted that these points are relevant and meets the best interest tests.
9. The Researcher explained that they estimate that around half of the people living in the community don’t come to services and don’t know that there are services.

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 clarified with the Researchers whether what they intend is to still ask everyone in the house, whether they are a carer or not, to do the carer bit even when after completing the assessment the main participant is found not to have dementia. The Researchers confirmed that this is their intention and that those people will be identified by the main participant and they are someone who will corroborate what is going on. A complete assessment is a dyad and the Committee queried in cases where a participant lives alone then they can’t get a complete assessment.
2. The Committee would like to see a process outlined in the event that abuse is disclosed and what the Researchers would do about that. In the past the Researchers have made sure that there is a protocol so that if this does happen staff know who to talk to. In NZ Age Concern is responsible for elder abuse. Please include these processes in the protocol.

The Committee requested the following changes be made to the participant information sheets and consent forms:

1. The proxy consent form submitted with his application states “I agree my relative can take part in the study”. It should rather state something along the lines of “I have been consulted and I am comfortable with the provider making the decision or that this is consistent with what I think the person’s wishes might have been”. They are not the decision maker and it is important that they are not expressed as such. The provider is the decision maker having ascertained that it is in a person’s best interests.
2. In relation to reasonable steps having been taken to ascertain the views of the consumer if a person says ‘no’ then that is respected and if the Researchers can’t do what they think the person wants then they consult someone interested in their welfare. The Committee asked that the Researchers revise the documents around consultation with the family for that small group of participants who cannot consent for themselves.
3. The Committee noted that carers are also participants in their own right. This is not clear in the information sheets. The Committee noted that one states there is an assessment and that it’s good for your family member to have an assessment. Please be clear about when you are seeking consultation with the family member in that small group of people who can’t consent that information sheet is about the assessment so that they can understand what they are being asked to do, i.e whether their family member would have wanted to be in the study.
4. The Committee also noted that the study questionnaires are extensive with personal questions and asked that they give indication in the information sheets about the type of questions that they will ask.
5. The Committee asked the Researchers to explain what they mean by “head of household” as this wasn’t clear. The Researchers noted that in some families the head of household will be the person who makes decisions about money and what happens in the family and that person is not necessarily the main carer of the person.
6. The Researcher noted that there are potentially three people being interviewed: the head of the household, then the main caregiver and the person who is being assessed. There is a different questionnaire for head of the household that mainly looks at household income, how many toilets there are in the house etcetera. With this in mind the Committee suggested that the term ‘Head of the Household’ be changed to something like ‘Family decision maker’.
7. The Committee noted that the primary participant has to consent to could fill out the household questionnaire. The Researchers noted that they are trying to cater for a number of situations. For example, it may be that the participant is independent, doesn’t have a care and, is the head of the household in which case they would do the head of the household and the individual assessment. This will be established in the relationship building before the interview. The Committee noted that it is not clear in the main participant information sheet that they may be asked to fill out other forms and the head of household PIS currently has information about the main participant’s assessment and seeking permission to the main participant’s assessment which is not a role that the head of the household can do.
8. The main PIS should cover all the things that someone may be asked to do. That would be questionnaires which may include questions about your household, it may include questions about your health for example and, that it may include carer giving information about you and about their own health. The Committee agreed that essentially the information sheets and consent forms are confused because people need to be clear about what they are consenting to.
9. The Committee noted that the Researchers have stated that study data may be used in future studies and asked whether this is for future unspecified research. The Researchers explained that they in collaboration with another dementia researcher and they would like to look at risk factors in NZ comparison with other low and middle income countries and the UK. The data will be de-identified. The Committee asked that the Researchers expand on this in the information sheet and that they include a statement for participants to agree to this in the consent form.
10. The Committee would like to see changes made to the protocol and a revision of the participant information sheets and consent forms. As the team is clear on the changes the Committee agreed that it would be happy to provisionally approve this application.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies, para 6.22)*
* Please update the study protocol to include more detail on study procedures. (*Ethical Guidelines of Intervention Studies, para 5.5*)

This information will be reviewed, and a final decision made on the application, by Ms Toni Millar and Dr Karen Bartholomew

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| **11** | **Ethics ref:** | **18/NTA/177** |
|  | Title: | Phase I/II pharmacokinetic multi-tumour study of subcutaneous formulation of Nivolumab monotherapy |
|  | Principal Investigator: | Dr Richard North |
|  | Sponsor: | Bristol-Myers Squibb |
|  | Clock Start Date: | 04 October 2018 |

Dr Richard North 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. This study is a phase I/phase II pharmacokinetic study. Nivolumab is a new immunotherapy drug and is similar to Keytruda.
2. This study will trial whether a subcutaneous (subcut) administration is as efficacious and therefore potentially of more convenience to patients.
3. Participation in this trial gives patients’ access to Nivolumab in NZ who otherwise don’t have access.
4. Other similar studies have shown that subcutaneous administration of the drug is equivalent and more convenient.

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 whether patients would have to pay for Nivolumab if they weren’t in this study. The Researchers confirmed that this is the case with one exception as Nivolumab is funded in New Zealand for Melanoma.
2. In relation to the study design the Committee noted that the Researchers will recruit to part A first and wait until that is filled up and asked whether it is possible that a patient could get randomised to part B first and then have to wait for part A to be filled before they get treatment. The Researchers confirmed that this is not a possibility and patients will not need to wait to get dosed.
3. There is an optional part on the consent form about interviewing patients about their experience with the subcut and the Researcher confirmed that this is optional. The Researchers don’t plan to action this as they haven’t seen the questions that the company want to ask. While it is likely to be about quality of life the Researchers acknowledged that more work is needed before patients go ahead. It is optional and doesn’t alter participation at all. The Committee asked whether the interview will be recorded. If yes, there will be confidentiality issues around that. At the moment it is not an issue as the company is still putting the interviews together. The Researchers will submit to HDEC for review once this is finalised.

The Committee requested the following changes be made to the participant information sheet and consent forms:

1. The people who will be able to view identifiable data will be the investigators and the study monitor. The sponsor, the lab and other third parties will only see de-identified data. Please make this clearer in the participant information sheet.
2. The Committee asked that the Researchers give the Pregnant Partner information sheet a complete review as it refers to gaining consent for information about the unborn child. The Committee noted that consent to use information about the child can only be gained after the child is born and this form will need to be reworded. Please also include Maori contact details and HDEC contact details.

Future unspecified research participant information sheet:

1. Page 4: The data protection section makes reference to the possibility of identifiers being sent to the sponsor on things like scans. The Researchers confirmed that only de identified information will be sent to the sponsor and they will amend the wording to reflect this.
2. Page 5: The Committee noted the statement that researchers may not be able to destroy samples as they may no longer have the identifier list. The Researcher explained that they take the view that it patients feel that now or in the future they might want their samples back they should not tick the optional box for future research as the researchers can’t guarantee return of the samples. Please reword this statement to reflect this.
3. The Committee noted that the HDECs have a new compensation statement for sponsored studies, which it would like to see in the information sheet and which some sponsors have indicated that they want to review before it is included in the information sheets. <https://ethics.health.govt.nz/>

PIS Intervention Study:

1. Page 8 of 24 under additional follow up states that visits will occur every three months, potentially more frequently, it may be necessary to go to your doctor’s office for additional scans. The Committee asked the that Researchers be more specific about the length of time that people will need to give to this study and why visits might be more frequent – i.e. because of clinical need. Please remove the sentence that participants may need to go to their doctor’s office for a CT or MRI as this is not practice in New Zealand. In the next paragraph please state will “ask you about various things” rather than “attempting to obtain information”. The second bullet point at the bottom of the page under the heading ‘What do I have to do?’ states “describe how you feel and possible side-effects will be discussed.” Please remove the words “will be discussed”.
2. Page 21: in relation to withdrawing from the study please be clear that people can also advise verbally that they don’t want to be in study anymore.
3. Some information about mandatory genetic testing is mentioned on page 5 and then mandatory biomarker testing. The Committee noted that this sounds like future unspecified use and the protocol talks about whole exome sequencing as a mandatory part. The Researcher explained that whole exome sequencing is in relation to the cancer not the patient and they are looking for issues within cancer that predict or fail to predict response rather than trying to work out whether a patients of a certain genetic sub type. The Committee accepted the Researcher is comfortable with the mandatory genetic testing part and queried whether they are comfortable with the biomarker part as what is written in the text sounds like future unspecified use. The Researcher is comfortable with this and explained that when they talk to patients they explain that it is a fishing trip and what they are trying to work out in who the cancer drug works and works best and that this involves genetic testing and if they are unhappy with that then they shouldn’t participate. Likewise with biomarkers. The Committee noted that the wording for biomarker testing is usually more specific and is also in the protocol but in this case it is not in either. The Committee requested that the optional unspecified use form not be called “additional testing”. Either say it is optional unspecified use or biorepository so that it is clearer to patients. The protocol states tumour tissue and it would be good to include this if the Researchers are intending that left over tissue goes into a repository.
4. Please state that tissue will be stored for 15 years rather than indefinitely.
5. Please update the advocacy email to read: [advocacy@advocacy.org.nz](mailto:advocacy@advocacy.org.nz)

Optional biopsy information sheet:

1. Page 1: patients will always be in a position where they can consent to this for themselves and the Researchers will not ask a relative or caregiver to consent on a patient’s behalf. Please make this clearer on the information sheet and remove the requirement for a witness to sign. The Committee would like to see more information about why optional biopsy process and why it is required. For example, that patients have already participated in the main study and the cancer has come back and we would like to collect another biopsy and we are asking your permission to do this.
2. Consent form: the end statement says that they accept to “perform” an optional biopsy and this should read that they accept to undergo an optional biopsy.

FUR PIS

1. Page 2 of 9 of the additional research participant information sheet: please state that once samples are sent overseas NZ law does not apply and the Researchers have no control over what happens to them.
2. Page 4: under the heading information data records that directly identify you please remove the paragraph about there being a possibility of re-identifying participants.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies, para 6.22)*

This information will be reviewed, and a final decision made on the application, by Dr Cordelia Thomas and Dr Christine Crooks.

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| **12** | **Ethics ref:** | **18/NTA/178** |
|  | Title: | A research project testing the performance of the ellume·lab Group A Strep test device compared to collecting swabs for culturing, in participants with strep throat (Acute Pharyngitis). |
|  | Principal Investigator: | Dr Barney Montgomery |
|  | Sponsor: | Sponsor Company |
|  | Clock Start Date: | 04 October 2018 |

Dr Barney Montgomery 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 ethical issues (resolved)

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

1. The Committee complemented the Researcher on a well-written participant information sheet and noted that it had some questions about it and about the application form.
2. The Committee asked whether the Researchers have consulted with the national programme for rheumatic fever and strep testing about this work. The Researcher has not consulted with them to date but in future if the study device works then they will talk with them about using it clinically. The Committee noted that this project is about group A strep but there is no mention of rheumatic fever and it’s a big programme in New Zealand. The Researcher apologised for not including more detail in the application but explained from their point of view the reason why this would be so good is it could prevent other complications of rheumatic fever and group A strep and that’s where the value lies.
3. The Committee asked how this test different from other strep point of care testing. The Researcher explained that the test is done slightly differently and there is slightly different technology in this test and it works faster and they want to find out how accurate this is. When reading previous tests is it hard to tell if the result is positive or negative. The Researcher noted that it is his understanding is that the test gives clear results.
4. The participant information sheet asks for permission to contact a participant’s GP but the Committee noted that most of the time they will already be with their GP. The Researcher explained that this depends on the way that participants come to the Researchers. If they haven’t seen their GP the Researchers will treat them and refer them to their GP with their permission.
5. Payment details mentioned in the application are for travel and will depend on how far participants have travelled and the Researcher noted that this will be in the ball park of 50 to 100 dollars. The Researcher advised that this is a flat rate and participants also have to reach other criteria to be involved and argued that this is not an inducement.
6. There is no script for the post-test phone that call that either nurses or the study co-ordinator will make to find out how the participant is doing and what the status of their health is. The Committee asked whether this phone call is relevant to study outcomes as they are just looking at concordance of the two tests. The Researcher agreed that it is not but as a duty of care they like to follow up and make sure people are okay. For participants coming through social media rather than referral by their GP then the study will give results and treat them. The Committee asked whether the Researchers will give participants antibiotics if they get a positive swab. The Researchers will prescribe for participants who come to them in that way.
7. The Committee queried the number of positive results needed to validate the test. 70 positive results are needed. The prevalence in New Zealand is not all that high and the Committee queried what population the Researchers intend to recruit. In a high risk community only 8% of throat swabs are positive and that is in children presenting with a sore throat in a school based setting. The Committee recommended that the Researchers think through their sample size and if they are swabbing European children the proportion that are positive will be lower. The percent of positive also varies by age and drops off quickly after age 14 so if the Researchers are wanting to increase their chances of finding strep then they might want to focus on the peak age of strep which is 9-12 year olds. At the moment with a n of 500 they might only find 40 and then their numbers will be too small and the Committee recommended that the Researchers carefully think through their sample size calculations.

Summary of ethical issues (outstanding)

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

1. Patient recruitment will be done in several ways. They will be identified through the Researcher’s clinic, colleagues’ clinics – people who present acutely with sore throat - and also reach out through social media. If people contact the Researcher via social media they come to the clinic. They will go to a page with screening questions then they will be phone screened with one of the researchers. They may or may not have seen their GP first. The Committee queried whether there will be a delay in accessing care. The Researcher’s aim is to see them on the same day. If they are outside of the study region the advice on the website is unclear. The Committee asked the Researcher to address this.
2. The trial will be operating trial from a private research site that is not attached to a medical centre so participants will be coming specifically for the trial to that site. The Committee asked the Researcher what the duty of care is if the participants don’t turn up at the research site. The Researcher explained that he would treat in the normal way before swabbing the throat as part of standard of care and they will get a second or third swab at the study site. If participants don’t turn up at the study site the Researchers would contact them and make sure they were treated appropriately. The Committee noted that what it doesn’t want to happen is kids at risk of rheumatic fever not turning up and missing out on treatment. The Researchers need to be clear in their protocol of their processes to make sure that high risk children are going to be safe and treated.
3. The Peer review submitted has been done by a consultant related to the company and is not independent. The Committee requested the Research team provide another peer review that is independent and suggested this could be done by someone involved in the rheumatic fever programme or a public health physician who has experience in treating patients with rheumatic fever.
4. The study investigator brochures states that this study is not a first in human study and that a trial has been done with 65 participants. It also says the results were sub optimal and there was a high failure rate but then doesn’t say anything about what was changed. The Committee asked whether there have been any changes to the product. The Researcher agreed that he would go back to the sponsor and then advise the Committee. The Committee noted that there is no point in doing the study if it is going to find the same results in more children.

The Committee requested the following changes be made to the participant information sheet and consent forms:

1. Section 15: please specify that health information will be collected and be specific about what information you will collect.
2. Page 5 mentions a unique identifier that includes partial date of birth. The Committee noted that partial date of birth is identifiable and asked the Researchers to use another unique code.
3. Please state that information will be kept for 10 years after the participant turns 16 rather than 25 which is currently stated.
4. Consent form: please include tick boxes for truly optional statements only. Please revise and remove yes/no boxes as needed.
5. The PIS does not mention that tissue is going overseas but r.3.7 in the application form states that swab will be stored and shipped for possible future testing. This is future unspecified research and as such requires a separate information sheet and consent form.
6. Section r.3.11 in the application form talks about setting up new tissue bank whereas other information in the application contradicts as it states they are not setting up a tissue bank. The Researcher advised that they have no intention of setting up a tissue bank and that this may have been an error on their part. He will check this and confirm for the Committee. The swabs will be sent to Australia where the company is based after testing in New Zealand to help them develop the device further. Please state this in the information sheet and if the swab will be used for future unspecified research an optional information sheet and consent form is needed. If Researchers intend to look at the bug and do genotyping of the bug this can be mentioned in the main form but if they are testing human tissue of any form then a separate information sheet and consent form is needed.
7. The Committee asked that participants be informed that they can withdraw from the study verbally and do not have to complete a form.
8. All research in New Zealand should collect ethnicity data unless there is a good reason why this cannot be done. Please change “race” to “ethnicity” in the participant information sheet and please collect according to NZ census criteria.
9. Please revise and tweak the study advertisement to more clearly reflect question. Currently it asks “do you want to know if antibiotics will help your child which is not the study question.

Decision

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

* Please provide evidence of favourable independent peer review of the study protocol (*Ethical Guidelines for Intervention Studies* Appendix 1).
* Please amend the information sheets and consent forms, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Please update the study protocol to include more detail on study procedures. (*Ethical Guidelines of Intervention Studies, para 5.5*)

This information will be reviewed, and a final decision made on the application, by Mrs Helen Walker and Dr Kate Parker.

## General business

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

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| **Meeting date:** | 20 November 2018, 01:00 PM |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

No apologies were tendered for this meeting.

The meeting closed at 6.45pm.