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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 20 February 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 12 December 2017 |
| 1.30pm | New applications (see over for details) |
|  | i 18/NTA/17  ii 18/NTA/4  iii 18/NTA/6  iv 18/NTA/7  v 18/NTA/8  vi 18/NTA/12  vii 18/NTA/20  viii 18/NTA/21  ix 18/NTA/22  x 18/NTA/23  xi 18/NTA/24  xii 18/NTA/26 |
| 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 | Lay (consumer/community perspectives) | CEN co-opt | CEN co-opt | Present |
| Dr Kate Parker | Non-lay (observational studies) | 11/11/2015 | 11/11/2018 | Apologies |
| Dr Nora Lynch | Non-lay (intervention studies) | NTB co-opt | NTB co-opt | 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 |
| Ms Rochelle Style | Lay (ethical/moral reasoning) | 14/06/2017 | 14/06/2020 | Present |

## Welcome

The Chair opened the meeting at 1.00pm and welcomed Committee members, noting that apologies had been received from Dr Kate Parker.

The Chair noted that it would be necessary to co-opt members of other HDECs in accordance with the SOPs. Mrs Helen walker and Dr Nora Lynch 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 12 December 2017 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **18/NTA/17** |
|  | Title: | Defining the chain of infection of ESBL-E. coli |
|  | Principal Investigator: | Dr James Ussher |
|  | Sponsor: |  |
|  | Clock Start Date: | 01 December 2017 |

Dr James Ussher 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 is a feasibility study of a larger planned case control study looking for risk factors that might contribute to transmission of extended spectrum beta-lactamase (ESBL) producing Enterobacteriaceae in urinary infections.
2. The intention is to check the representativeness and effectiveness of recruitment method, refine contents of questionnaire and generate data for a sample size calculation.
3. Case Population: 20 ESBL-E.coli UTI sufferers identified by the Co-ordinating Investigator in his role as microbiologist at Southern Laboratories. Includes minors.
4. Control population: 20 non ESBL-Ecoli UTI sufferers from the same lab. Includes minors.
5. Recruitment procedure is a letter of invitation from the Co-ordinating Investigator in his clinical lab role. The Committee noted it was well written.

Summary of ethical issues (resolved)

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

1. The Researcher(s) stated they would exclude patients from rest homes and anyone who could not provide consent.
2. The Committee noted the potential for some reporting to be stigmatising but acknowledged the researchers plan to minimise this by talking with relevant communities first (for example if shell fish are found to be a source of contamination for certain communities) (app page 16). This is appropriate data risk management and it is good to see the researchers are aware of these possibilities.

Summary of ethical issues (outstanding)

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

1. The Committee noted that the questionnaire which will be administered over the telephone is very long, and asked whether children would be able to manage the duration (estimated to be 60 minutes). The Researcher(s) stated that this was a feasibility study, so part of the study would be to consider that, but noted that this part of the study may only be completed by older children. The Researchers added that, at this stage, they did not want to rule out younger children participating if they wanted to. The Committee and the Researcher(s) noted that parents could assist younger children if required.
2. The Committee noted that receiving a telephone call when potential participants have actively ignored 2 previous letters may feel like harassment and a potential participant should not have to respond 'no' to a letter to avoid this telephone contact. The Researcher(s) acknowledged this point. The Committee suggested changing the process for contacting potential participants to mitigate feelings of harassment.
3. Please provide assent documents for 7-11 and 12-15 year olds. Provide a participant information sheet targeted at the parent or guardian of <16 year olds. The Committee noted currently only PISC for > 16 has been uploaded. The Researcher(s) noted they would provide these forms.
4. The Committee noted that the participant information sheet states questionnaire data will be 'anonymized'. However, data entered into Redcap database includes month and year of birth, full street address and full work address. This is fully identifiable. Please justify the collection of addresses and consider collecting only age. The Researcher(s) explained that it would look at geographical clustering, and whether that could be done by GPS co-ordinates, but this does not get around the issue. The Committee noted it should be possible to have relevant data without the address in the database. For example, mesh block.
5. Please provide the interviewer narrative for oral consent at the start of the interview for those who have not returned the consent form.
6. The Committee asked for a documented management process if a clear pattern of a common infectious source (food store or eating place) emerges in the cases. The Researcher(s) stated such patterns would be unlikely given the numbers in the study but would rely on the expertise of the researchers on the team who would be able to identify and act on any patterns. The Committee noted this could be added to the protocol.
7. The Committee noted that this is a huge questionnaire, and queried whether researchers have given thought to offering a voucher as koha which may assist with recruitment in this and the definitive study.
8. The Committee asked about the data access and linking part of the study. The Researcher(s) explained that they want to send NHIs to the Ministry of Health, some for those who participated in the research and some for those who hadn’t participated in the research (ie, who had not consented or who had not replied to the research), in order to assess whether there was any bias in the recruitment. No consent to the use of NHIs in this manner would be sought. The Ministry would return demographic information, but no NHI or identifiers. The data will be compared with real participation to assess similar response rates between groups, for example Maori and Pacific Island participation, and whether this recruitment is suitable for these populations. The Committee approve a waiver of consent for de-identified demographic data on non-participants in this case

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

1. Page 2, contacting you – be clear this is for a phone interview.
2. ‘what are my rights’ – amend and clarify whether the data collected is de-identified (coded) not anonymised Similarly with statements made under the heading “What will my participation in the study involve?”
3. The PIS states that no identifiable data will be collected, but this is clearly not the case, please remove.
4. The application says the data will be de-identified and data stored under a study number. This is not anonymous. If the data is to be anonymised, then it is not possible to withdraw from the research (as currently stated in the PIS and consent form). Please amend both the PIS and the consent form to accurately reflect the identifiability of the data and rights of withdrawal.
5. Suggest remove the statement ‘looking for funding’ as that isn’t relevant to these study participants.

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 Observation Studies* *para 6.11*).
* Please provide age appropriate assent form for non-consenting (children) participants to sign (*Ethical Guidelines for Observation Studies 6.21)*
* The study design must minimise risk of harm, please address outstanding ethical issues in a cover letter and by amendments to the protocol (*Ethical Guidelines for Observation Studies* *para 5.5*).

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

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| **2** | **Ethics ref:** | **18/NTA/4** |
|  | Title: | Nasal high flow oxygen |
|  | Principal Investigator: | Dr Alison Pirret |
|  | Sponsor: |  |
|  | Clock Start Date: | 08 February 2018 |

Dr Alison Pirret 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. This is an observational study in which the proposal is to prospectively collect data for at least 72 hours (and then later on length of stay/outcome of stay from the records) of a specific cohort of hospital patients (acute on chronic respiratory failure or decompensation) who are receiving high-flow nasal oxygen in a ward setting.
2. There will be multiple hospitals involved but only hospitals with access to specialised nursing teams to respond to rapidly deteriorating patients and only wards which routinely use this therapy will be included.

Summary of ethical issues (resolved)

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

1. The Committee asked why the prior study was not considered generalisable. The Researcher(s) explained that it involved use of standard data collected and was about internal practice evaluation, which had been in place for 8 years. The Researcher(s) explained the escalation procedures in place at the hospital, and the well-developed procedures, monitoring and staff. These reasons are why the prior study results were not applicable to other centres.
2. The Researcher(s) reiterated that no new observations, no new interventions, for the study. The Committee noted that while most of the information is routine, it is not necessarily collected in a routine manor.

Summary of ethical issues (outstanding)

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

1. The Researcher(s) explained that the prior study, which was non-consented, went through the research office and was not deemed in scope for ethics.
2. The Researcher(s) explained that for this study there is no change in practice. The study is not an intervention study because the participants are already receiving high-flow nasal oxygen.
3. The research involves collecting and accessing data.
4. The Committee asked why there is no randomised controlled trial planned, given that effectiveness is claimed as a study endpoint. The Researcher(s) explained that it would not be ethical to do it, due to evidence that the standard practice of using high flow nasal oxygen improves outcomes. The Researcher(s) stated that they do not think that not providing it, by way of placebo or control arm, would be ethical.
5. The Committee noted that evidence would be generated by an RCT to support this view, as anecdotal information and observational studies cannot answer comparative effectiveness. The Researcher(s) stated that such research could be done in Australia where the use of high flow nasal oxygen is not as common.
6. The Committee noted effectiveness cannot be determined, as far as clinical outcomes, compared to other clinical groups in this study. The Researcher(s) stated the ‘before and after’ design provides some degree of comparison.
7. The Committee raised questions around the Researcher(s)’ analyses and outcomes. The Committee noted the three primary outcomes, and asked whether the Researcher(s) adjusted either the sample size or the significance level for the effects of multiplicity. The Committee noted the Researcher(s) state the sample size was calculated using an 'effect size of 0.8' and asked which outcome this refers to and whether that means a 20% difference in that variable (before and 1 hour after NHF O2 implementation). Please address these queries.
8. The Committee expressed concerns around the study design, particularly the lack of control, if claims of efficacy and effectiveness were to be made. The Committee noted that for the first three outcomes, drawing conclusions with the current design may be possible, but the fourth outcome is unlikely to be able to be met. The Committee noted observed improvements or changes to length of stay could be related to antibiotics and other confounders, for example. The Researcher(s) disputed that the kinds of observable improvements could be attributed to antibiotics. The committee requested further information on how the study endpoint of effectiveness would be determined, or consider reframing as descriptive.
9. The Researcher(s)’ plan is to obtain consent retrospectively when the patient is stable. Patients who die will have their data retained for scientific validity of the study. It is not clear what will happen to the data of patients who live but decline to provide written consent.
10. The Committee discussed with the researcher their concern about ability to have informed consent (even if relatively low risk as data collection) in the situation of acute respiratory distress/illness.
11. The Committee stated that because this project hinges on prospective data collection, potential participants should be offered brief information about the research at the time consent is sought from the patient to receive treatment in the form of high flow nasal oxygen. The Committee stated that: (1) dissent must be respected; and (2) verbal consent should followed up by a re-affirmation of consent in writing as soon as the patient has stabilised. The Committee requested the Researcher(s) develop a brief paragraph to be read to patients to obtain verbal consent to prospective collection of data for research, noting that this consent method was appropriate because while the data was relating to standard of care, though it was protocolised and formally collected (result in more specified time points and
12. The Researcher(s) confirmed that all data was standardly collected. The Committee asked whether data could be pulled by file, after consent. This should be possible if all data is routine. The Researcher(s) explained that while it is all usually collected, there is variance around how it is recorded due to local practices, and this is a multicentre study. The Committee noted that because it is protocoled it would be research, opposed to auditing the data locally.
13. The Committee asked about recruitment. The Researcher(s) explained if ICU or PA nurse is called to see a patient, and if the patient is deemed to benefit from nasal high flow, those individuals would be a potential participant. The Researcher(s) would tell them about the study and if they would have their data in the study, noting nothing is done differently whether they participate or not.
14. The Researcher(s) explained they would ensure there is adequate resourcing to manage the consenting.
15. The Committee noted that consent must be prior to the nasal flow or any study data collection.
16. The Committee noted option for verbal consent. The Researcher(s) noted that verbal consent is given for applying the intervention in the clinical context.
17. The Committee queried how identifiable data sheets would be returned to PI from participating hospitals. Please address this in a cover letter.
18. Collect ethnicity according to 2013 census categories.

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

1. Include a sentence describing NHFO2 in the 'Purpose of Study' section.
2. Make it clearer in the 'Participation" section that nothing changes about treatment, you would be having the intervention (oxygen) anyway, nothing will change about your care whether you participate or not, this is just about data collection and use - similarly, in 'Risks Benefits' section, the focus should be on risks of data abuse not on risks of NHF O2 which is not a study variable. Reword this section to remove this.
3. Under 'Rights' add the right to see and correct collected data.
4. "Contacts': add Maori contact details
5. Consent form: remove tick boxes from non-optional items
6. In both the PIS and the consent form please amend statements which suggest that there will be no material that could identify participants to wording which reflects that information will not be published in a form that could reasonably be expected to identify participants.

Decision

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

* A verbal consent process must occur due to observational data collection, while not new data, it is formalised and differs from ordinary care, some of which could be considered study data. (*Ethical Guidelines for Observation Studies* *para* 6.1)
* Scientific validity and merit must be met in order for risks to be justified (*Ethical Guidelines for Observation Studies* pg.31)
* The study design must be scientifically valid and outlined in a complete protocol (*Ethical Guidelines for Observation Studies* *para 5.5*).
* Please amend the information sheet and consent form taking into account the suggestions made by the Committee (*Ethical Guidelines for Observation Studies* *para 6.11*).

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| **3** | **Ethics ref:** | **18/NTA/6** |
|  | Title: | Decision-making in the Child Protection Alert System |
|  | Principal Investigator: | Dr Patrick Kelly |
|  | Sponsor: | Auckland District Health Board |
|  | Clock Start Date: | 08 February 2018 |

Professor Fred Seymour, Dr Carmen Basu, Miranda Ritchie, Selina Moore, Andrew Thompson 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 is a mixed methods observational study of how multidisciplinary teams (MDTs) work in different DHBs when they consider whether to place a child notified to Oranga Tamariki (ie, who has had a “Report of Concern” made) on the National Child Protection Alert (NCPA) system run by DHBs since 2011.
2. This research was initiated because of prior study evidence of inconsistencies between DHB teams, in how many of the cases discussed at MDT meetings receive an Alert, and in differences of understanding between members of MDTs about the functioning of the NCPA system.
3. Eight DHBs will be chosen ‘randomly’ to participate in the research, 2 per quartile from the Chan study.
4. Research participants will be members of the MDT teams (3-7 depending on the DHB) and must all consent to 2 of the researchers sitting in on 2 MDT meetings, the second of which will be audio-taped and videoed.
5. The Researchers(s) propose that if 1 member of the MDT does not consent, s/he will be excluded from the meeting. If more than one member of the MDT does not consent, the DHB will be dropped from the study and replaced by another in the quartile.
6. Two MDT members, selected at random by drawing a blue marble from a bag, will be asked to do a semi-structured interview about their experience at the videoed meeting which is to take place within 72 hours of the meeting.
7. During the MDT meetings researchers will be privy to information about individual children/young persons (CYP). However, neither the CYPs nor their parents/care givers will have consented to the disclosure of information about the CYPs to the researchers. However, all details which would identify the CYP will be expunged from the video and audio transcripts and the video will be destroyed.
8. Furthermore, a justification for non-consent by the CYP and/or their parents/caregivers is available pursuant to clause 6.43 of NEAC’s Observational Guidelines on the basis that the procedures required to obtain consent are likely to cause unnecessary anxiety for those whose consent would be sought. Depending upon the individual circumstances, this could apply to both the CYP and/or the parent/guardian because seeking consent could compromise their welfare and best interests in being kept safe. New Zealand’s regulatory framework strengthens information sharing provisions to keep vulnerable CYP safe from harm and emphasises that the welfare and best interests of a child in his or her particular circumstances must be the first and paramount consideration and one of the key principles in making that determination are that a child’s safety must be protected from all forms of violence from all persons, including members of the child’s family, family group, whanau, hapu, and iwi
9. Stigmatisation is a potential disadvantage to the CYP or his/her or relatives or collectives (clause 6.43(b)). However, the Tone research suggests more than half of the respondents disagreed that the CPAS stigmatised families. In any event, any stigmatisation would likely have first resulted from a “Notification of Concern’ to Oranga Tamariki and the decision to place an alert, which would happen irrespective of the research. Accordingly, provided the research findings are published with great caution, the risk of stigmatisation should not be increased by the research. Indeed, the study should ultimately reduce the risk of stigmatisation by improving an understanding of the factors that influence decision making in the MDTs to put on an alert.
10. Clause 6.43 (c ) would appear to be satisfied given the public interest in protecting vulnerable children and strengthening the NCPAS against the remote possibility that individual children/young people will be identified beyond the research team and the MDT which The Committee think it unlikely given the manner in which the de-identification of the CYPs will be undertaken
11. The Committee noted the three peer reviews, including a former Children’s Commissioner.

Summary of ethical issues (resolved)

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

1. The Committee asked how and when consent of the MDT members will be taken. The Researcher(s) explained consent forms are issued in advance. There will also be a meeting with each of the MDT members to collect forms and answer any questions that arise. The Committee suggested that the selection of the two MDT members to take part in the semi-structured interviews should take place outside the group setting to mitigate identifiability of those members who are being interviewed.
2. The Committee asked what happens if one person states they do not want to consent. The Researcher(s) explained they can absent themselves from the meeting, however if their absence meant the review would not occur, for example if the paediatrician declined consent to the researchers’ attendance at the meeting, the DHB would be removed from the study. The Researcher(s) emphasised that appropriate functioning of the MDT meeting was a paramount concern and they did not wish their research to result in the exclusion of any member who would have significant or valuable input into the cases to be discussed at the MDT meeting.
3. The Committee asked how the Researcher(s) intended to protect MDT members from pressure to participate, for instance from the Chair or other members. For example, what would the Researcher(s) do consent was obtained at the start of the first meeting and one member did not wish to participate in the research? The dissenting MDT member could be stigmatised, especially if more than one MDT member declined and the researcher could not proceed at the DHB. The Committee also asked about the potential for reputational damage for individual MDT members, for example, regarding their decision to participate (or not) in the research. The Researcher(s) explained that when they first attend the DHB to talk with MDT members about the research, it will not be videotaped. The Researcher(s) noted the participant information sheet is strongly worded around participation being voluntary, and expressed the hope that the opportunity to decline participation in the research could be openly given without fear of reputational damage. The Committee noted that participation in the research cannot be said to result in no risk of reputational damage, but it noted the steps the Researcher(s) intend to take to mitigate any such consequences.

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 about potential bias introduced by dropping and replacing DHBs with > 1 decliner. The Researcher(s) explained that the first meeting is to settle and minimise any changes, but acknowledged the impact of the Researcher(s) presence will not be able to be totally removed. The Researcher(s) noted the potential for this method of enrolment to affect randomisation procedures. The Committee queried how will this work in practice if Researcher(s) travel all the way to a DHB and someone declines. The Researcher(s) acknowledged that selection of DHBs wasn’t really random but targeted.
2. The Researcher(s) explained that the meetings take priority, not the research.
3. The Committee asked about processes for data confidentiality, in relation to video and audio. The Researcher(s) confirmed the video recording will be destroyed but they plan to store the audio recording for 20 years. The Researcher(s) explained that was normal practice. The Committee disagreed. The Researcher(s) explained transcribing is not perfect. The Researcher(s) explained they usually destroy written and audio at the same time.
4. The Researcher(s) stated that they had not intended to give participants in the semi structured interviews the opportunity to self-review their transcripts, however they did not rule it out and would consider it as an option. The Committee noted this would assist with accuracy and go some way towards mitigating privacy concerns such as comments which might identify a participant despite the Researcher(s)’ attempts to de-identify or anonymise the transcripts.
5. The Researcher(s) explained the security of storage of files (2 levels of code, plus police swipes etc.).
6. The Committee asked who the transcribers are. The Researcher(s) noted the transcriber has extensive experience with sensitive information and has been used by the Reseracher(s) on previous occasions with no concerns being raised. The transcriber will provide a confidentiality undertaking.
7. The Researcher(s) confirmed audio will be destroyed.
8. The Committee asked the Researchers(s) to review the scales used in the Likert-scale questionnaire which changes mid-way through from a scale of 1-5 to a scale of 1-7. Please make the scales consistent throughout the questionnaire.

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

1. Participant information sheet for group meeting and Individual Interview - add logo, lead researchers name and contact and HDEC approval slot to front page of both PISCs
2. Inform group members that if 1 declines to participate he/she will be excluded from their team meeting. If> 1 declines, the MDT meeting will be dropped from the study
3. Develop a proper participant information sheet for interview including some information about what will happen in the interview etc. Don't just include it on a consent form
4. Remove the data collection panel (ethnicity, role, experience, and gender) off the Group Meeting Consent form as this is not the appropriate place to collect data.
5. The Committee noted that the PIS should provide details of the kind of future projects the data may be used for (as stated in the app, page 16).
6. The Committee noted, for both the PIS and the consent form, that it is not possible to say that “no material that could identify any participant or patient will ever be published in any format”, particularly when brief verbatim quotes may be used in reports or presentations. The most that can be stated is that the information will not be published in a form that could reasonably be expected to identify the individual concerned. The Committee noted that providing interviewed participants the opportunity to review their transcripts will mitigate some of the risk of unexpected or undesirable attribution of quotes in published works
7. Similarly, given that statements made by interviewed participants may be attributable to them despite the Researcher(s) taking steps to de-identify them, please amend the statement in the PIS which states that involvement in the study ‘ will in no way after your employment , or the conditions of your employment’. It is possible that there could be employment consequences for the interview participants if they are identifiable.
8. The Committee asked whether the Researcher(s) will identify DHBs either in your initial report back to each DHB or in publications. If they will, please include this information in participant information sheet.
9. Please amend the consent form and PIS to note that audio records will also be destroyed after 20 years.

Decision

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

* Scientific validity and merit must be met in order for risks to be justified (*Ethical Guidelines for Observation Studies* pg.31)
* The study design must minimise risk of harm through good design and data management. Update the protocol taking into account suggestions from the Committee (*Ethical Guidelines for Observation Studies* *para 5.5*).
* Please amend the information sheet and consent form taking into account the suggestions made by the Committee (*Ethical Guidelines for Observation Studies* *para 6.11*).

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

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| **4** | **Ethics ref:** | **18/NTA/7** |
|  | Title: | (duplicate) SPAR |
|  | Principal Investigator: | Assoc. Professor Michael Jameson |
|  | Sponsor: | Australasian Gastro-Intestinal Trials Group |
|  | Clock Start Date: | 08 February 2018 |

Assoc. Professor Michael Jameson was not 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 Study

1. This is a resubmission of a study reviewed 2017, declined after provisional approval as requests around participant information sheets for future unspecified research were not met.
2. The Phase 2 study randomises 222 NZ/Australian rectal cancer patients to 90 days of simvastatin 40mg or placebo, starting a week before they begin pre-op chemo radiotherapy. The primary outcome is the proportion of favourable grade results on preoperative MRI with many secondary outcomes including reduced treatment toxicity.
3. There is data from observational studies which suggests simvastatin may confer tumour control and toxicity reduction benefits.

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 they did not have any issues with the study design and noted the response from the researchers.

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 the Main PISC still contains a lengthy explanation of future unspecified research which may include genetic research, none of which is required to meet the terms of this specific study. This should be removed, as it is outlined in the new future unspecified research document. The main participant information sheet can refer to the new document.
2. The Main PISCF consent form also states that by signing, consent for such extended research is being given. This must be removed and the consent for this be limited to the FUR PISCF
3. The Committee would accept a sentence in the Main PISC referring to the fact that participants will be offered a second PISC outlining FUR including genetics, which is optional for them to participate in. Everything else under the heading "Optional Extended Research including Genetics' needs to go, as does reference to ER /Genetics on the Consent form. This includes the statement of tissue retention for 10 years or until used up and reference to reapplication to ethics at 10 years. This is all in the future unspecified research already, which is where it belongs. The paragraph on Maori tissue beliefs should be retained and moved into "Required Research".
4. The Committee noted that the withdrawal form must be optional. Withdrawing from the study does not need to be in writing, and can be verbal. Participants should be informed in the new format of this.
5. In addition, the contraception wording needs to follow the HDEC template, see Template for reproductive risks in participant information sheets at <https://ethics.health.govt.nz/>
6. The PIS should mention what will happen with incidental findings and whether or not the participant's health care professional will be contacted (also include in the Consent form).
7. Add that tissue is going overseas.
8. Check that all of the documents have compensation provisions.

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 following information will be reviewed, and a final decision made on the application, by Dr Catherine Jackson and Dr Brian Fergus.

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| **5** | **Ethics ref:** | **18/NTA/8** |
|  | Title: | The Beta-Lactam Infusion Group (BLING) III study |
|  | Principal Investigator: | Dr Shay McGuinness |
|  | Sponsor: |  |
|  | Clock Start Date: | 01 February 2018 |

Dr Shay McGuinness and Mrs Rachel Parke and were present by teleconference for discussion of this application and Mrs Magdalena Butler in person.

Potential conflicts of interest

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

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

Summary of Study

1. This is an ICU - based Phase 3 randomised active control study looking at whether continuous infusion or intermittent (3-4 hourly) IV dosing with antibiotics gives the lowest 90 day mortality in critically ill patients.

Summary of ethical issues (resolved)

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

1. Standard of care is intermittent IV infusion, although continuous is in practice in some settings. The key ethical issue is the proposal to randomise unconscious participants to a treatment arm without consent.
2. Documentation has been submitted outlining relative/friend assent and participant ongoing consent. If the participant declines consent when competent, they will be asked to sign a document headed 'Revocation of Consent". However, this is misleading as one cannot revoke an instruction that was never given in the first place. The Committee requested that the wording is amended.
3. The Researcher(s) explained that the study is about the administration method of antibiotics, in relation to time dependent dosing to kill bugs or having a dose retained to kill the bugs. The Researcher(s) explained that there is a lot of evidence in favour of continuous delivery, however there is no definitive evidence to support better outcomes one way or the other. The Researcher(s) explained the prior studies Bling I and II. Bling I was single centre, Bling II was completed four years ago, with 5 of 6 participating sites in New Zealand.
4. The Researcher(s) stated this study will definitively say whether continuous or intermittent is better than the other. In ICU, patients will receive one of the other.
5. The Researcher(s) stated this study will definitively say whether continuous or intermittent is better than the other. In ICU, patients will receive method of antibiotic delivery or the other.
6. The Researcher(s) confirmed that the arms are two current usual standard of care options.
7. The Researcher(s) explained that the potential participants are all patients in intensive care. Some patients will be sedated and unable to give consent to the research while other patients will be conscious but insufficiently competent to provide full consent to the research. There may be a very small group of patients who may be fully competent to consent to the research and they will be consented prior to the research intervention. The Committee noted and commended the table provided by the Researcher(s) which describes the different types of patients likely to be encountered in ICU and proposes ways of dealing with each of them in terms of obtaining consent which include speaking to the patient (if possible) to ascertain his/her wishes regarding the research and speaking with family/friends (if available) to ascertain the patient’s likely views about research participation (consistent with Right 7(4) of the Code of Patients’ Rights).
8. The Committee asked the Researcher(s) to justify the research in terms of the requirement in Right 7(4) that the research be in the best interests of each enrolled patient. The Researcher(s) said that inclusion in the research would be in the best interests of each patient because s/he would receive the correct dose of antibiotic at the correct time. Some Committee members did not accept that the poor administration of antibiotics in clinical care and the failure to meet standard practice provided an inclusion benefit in ICU contexts where nurse to patient ratios are 1:1 and where antibiotics would be administered correctly irrespective of the research. In the study, the study procedures would involve increased oversight. Other members accepted that, in this particular study, it was likely that increased monitoring of the participants would occur which would provide a benefit for being in the research thus justifying it on the grounds of being in the best interests of the patient.
9. The Committee noted also that a consideration of what is in a participant’s best interests may be viewed in a more holistic manner than restricting interests to direct medical benefits. A holistic view of the best interests of each participant would include psychosocial issues and a consideration of the participant’s values and beliefs and different cultural, religious and social perspectives (Right 1, Code of Patients’ Rights). For example, a participant may have strong beliefs of altruism. These types of interests can be ascertained from either the patient, if s/he has capacity, or from family/friends who are available to speak about the patient’s likely views about research. The Committee also noted, that, taking all factors into a balance of what is in a participant’s best interests might also include whether the research poses a risk of harm to a participant and, if so, the nature and degree of such harm. In this study, there appears to be no risk of harm to participants.
10. The Researcher(s) responded to questions about comments made by some of the peer reviewers who questioned whether there was clinical equipoise. The Researcher(s) explained that while clinical differences had been indicated by the previous Bling studies, they were not statistically proven. This study will produce statistically significant differences that will prove the clinical differences identified in Bling II.
11. The Committee asked whether conducting the study with only participants who could give consent would reduce the study numbers and impact on the feasibility of the study. The Researcher(s) stated that while that would reduce study numbers it could be managed by recruiting for longer or studying a larger group. However, the main reason for wanting to include participants who could not consent is because those who are most unwell are a different patient population, with unique physiology etc and it is important to conduct the study with those patients as they have higher mortality.
12. The Committee noted that a Cochran review disputed the claim that people in clinical trials (broadly) do better. The Researcher(s) acknowledged this but noted there was evidence that people in ICU did do better if the ICU unit had a research focus.
13. The Researcher(s) expressed disappointment that standard of care for antibiotic administration is often not met because wrong doses are given and/or antibiotics are not given at the correct time. The Researcher(s) noted the Ministry of Health and DHBs are investing a great deal of resource into managing the inappropriate use of antibiotics issue including the increasing tolerance of bacteria to many antibiotics. The Researcher(s) it to try fix this so there is evidence is there for the study to in fact benefit individuals. The Researcher(s) explained argument is not great, and that kind of argument should be used sparingly, and in antibiotic trials, this is something that is significant for individuals.
14. The Committee and the Researcher(s) discussed best interests, noting the different types of benefits and the consultation with family to support making decisions in the interests of that individual.
15. From a social licence perspective, the Researcher(s) explained that they had research which showed this patient population’s willingness to be in research, stating that 400-500 patients in a cardiac ward were asked about their participation in research and over 80% wanted to participate in research of this sort. In particular, they were interested in participating in research which extended beyond new medicines to research which sought to ascertain which of commonly used treatments might be better and which the participants would be exposed to anyway. The Researcher(s) reaffirmed that the vast majority of participants in this survey wanted to participate in the research when given the opportunity to do so. The Researcher(s) also noted that with regards to people recruited without consent, when they were subsequently asked whether they would consent to the use of their data, the proportion who declined consent was well under 5% (most studies show a decline rate of under 1%).

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 the protocol has not been uploaded (only a summary of changes of the protocol). The protocol will require uploading. The Researcher(s) noted this was an error.
2. More work is needed on the three different versions of the PIS, the consent forms and the questionnaires.
3. Please include a statement that data is being shared and sent to Australia.
4. Note that for some of the PIS and consent forms the statements that GPs or other health professionals will be contacted to be informed of any concerns about [my] health or well being may need to be amended depending upon which situation is relevant – eg, it may need to be changed to ‘the person whose welfare I am interested in, [name]”
5. Delete in PIS’ and consent forms the statements ‘*no material which could identify participants will be used in any reports on this study*’ and replace with “*will not be published in a form that could reasonably be expected to identify …* “ The whanau/family consent form and PIS’ will need to be amended to: “will not be published in a form that could reasonably be expected to identify the person whose welfare I am interested in [name]”

The Committee noted there are at least four situations which need to be addressed in PIS’ and consent forms:

1. Where the patient has capacity and consents to enrolment in the research prior to the intervention
2. Where the patient is enrolled without consent due to incapacity (and either scenario 3 or 4 below applies) and the patient subsequently regains capacity and consents (or declines) further/continued participation
3. Where the patient is enrolled without consent due to incapacity but only **after** the researchers have spoken to a person interested in his/her welfare who is available and who advises the researchers of the patient’s likely views about participation in research and the researchers determine the research is in the person’s best interests
4. Where the patient is enrolled without consent due to incapacity and no person interested in his/her welfare is available for the researchers to talk to prior to enrolment and the researchers determine the research is in the person’s best interests and, subsequently, a person interested in the participant’s welfare is available and advises the researchers about the participant’s likely views about (continued) participation in research

The PIS which covers **continued participation and is addressed to the patient/participant** needs to be amended by inclusion of a statement in the first paragraph to the effect that:

*In all the circumstances, a decision was made to enrol you in the research because we considered that it was in your best interests. We took reasonable steps to find out what you thought and either we were able to do so and we formed the view, on reasonable grounds, that participating in the research was consistent with your views, or, we took into account the views of people interested in your welfare who were available to advise us at the time you were enrolled in the research”*

**The family/whanau PIS** needs to be amended in a number of ways. First, suggest delete the sentence ‘we believe it is good practice to talk with the relatives …” – the Code of Patients’ Rights requires it (Right 7(4)).

Secondly, instead of drafting two PIS’ for the two different situations for families ((a) where families are available and talked to before the patient is given antibiotics and enrolled in the research; and (b) where families are not available and the patient is given antibiotics and enrolled in the research but the families subsequently become available), the Committee suggests the whanau/family PIS include a paragraph after the second sentence under the heading “why am I being given this information” to the following effect:

*There are two different reasons why we would like to talk to you.*

* *We are about to give the patient whose welfare you are interested in antibiotics to treat his/her infection. We need to talk with you and take into account your views about whether or not the patient should be enrolled in our research. We also need to consider whether it is in the best interests of the patient to be involved in the research. Once the patient has full capacity, we will talk with him/her to obtain consent to ongoing participation in this research; or*
* *Because we could not talk with anyone who was interested in the welfare of the patient at the time we needed to give them antibiotics to treat their infection, we gave them antibiotics. We also decided that it was in his/her best interests to include them in our research and they have been participating in it. We would now like to talk to you to take into account your views about whether the patient should continue to participate in the research. Once the patient has full capacity, we will talk with him/her to obtain consent to ongoing participation in this research.*

1. The rest of the whanau/family PIS will need to be checked very carefully to make sure the two different situations are correctly worded – one will be for talking to patients who have not yet been enrolled and the other for patients already enrolled.
2. The Committee noted that the application (page 15) says the research involves no surveys or questions but there is a follow-up telephone call asking QUALY questions. This questionnaire will need to be amended if the interview is not with the participant. If family members are answering the questions, there are two different scenarios:
3. The family member has been chosen by the participant to answer the questions (which is the situation contemplated by the PIS) which provides consent for the family member to answer the question.
4. The family member has not been expressly chosen by the participant (who may still not be fully competent). The difficulty in this situation is that the family member has only indicated the participant would likely wish to participate in the research. In the absence of specific consent from the participant, the family member has no authority to answer QUALY questions about the patient/participant. The Researcher(s) should address how they intend to deal with this situation.

Decision

This application was *provisionally approved* by vote, with 6 for and 2 against, 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*).
* Provide further information on the study design, *in particular submission of the full protocol* (*Ethical Guidelines for Intervention Studies para* 5.4)

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

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| **6** | **Ethics ref:** | **18/NTA/12** |
|  | Title: | Mana Rangatahi |
|  | Principal Investigator: | Dr Kahu McClintock |
|  | Sponsor: |  |
|  | Clock Start Date: | 08 February 2018 |

Dr Kahu McClintock 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 is a pilot study set up to examine the content suitability, efficacy and implementation of a kaupapa Maori mental health intervention for 12-18 year old school students with social or mental health issues identified by the staff of their school. Content is intended to be tikanga based cultural education and reconnection, and to be strengths and resilience focussed.
2. It is to be delivered by Te Puna Hauora, a Bay of Plenty kaupapa Maori Health Trust. It has been trialled in 3 schools previously in an informal way without outcome data collection. The clear need for better Maori mental health services for youth, and the 'by Maori for Maori' approach are well articulated and accepted.

The Committee noted it is unclear what the design of this study – some places in the application, protocol and PIS refer to evaluation, some to intervention, some to participant action research. The committee requested clarity around the study design, as this has ethical implications and needs to be explained to participants.

1. Participants: N=40;20 participants 12-18 years from each of 2 Tauranga schools, not yet named. The participants will be identified by the school as having a mental health issue.
2. Outcomes: Does the cultural content of the programme improve Maori student’s wellbeing? Do programme contents improve Maori youth mental health? Which cultural contents do youth find most helpful? What in the overall programme do youth find most helpful? The Committee noted how these outcomes will be measured is not stated, it would have expected to see tools e.g. interview questions or questionnaires.
3. Recruitment: School staff refer participants to the programme. The Committee queried if this was a counsellor or any concerned teacher. It was unclear how the children and their parents/guardians will be approached for consent / assent and by whom.
4. The Researcher(s) explained that the school, alongside the parents, are involved as a collaborative. Teachers will be involved in the programme, working with researchers. The lead teacher will raise any issues with family, students themselves, and explain that there is a programme that is offered to help with those issues, which is voluntary.

Summary of ethical issues (resolved)

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

1. The Committee asked about data security. The Researcher(s) stated they ensure that they back up data, and explained that their organisations are mental health services, which are most sensitive, adding the host institution has been in this area for over 20 years.
2. The Committee queried if there was a memorandum of understanding or any agreements with schools. The Researcher(s) stated not yet, adding nothing had been started with regards to the study. The schools know of the service but are not aware of the study. The ethics process is being undertaken first.

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 details are unclear but it is stated that focus groups and interviews will be included. The framing principles of respect / face-to -face interaction/look-listen-speak/beneficence/caution/humility are grounded in Maori custom. Please elaborate in Protocol.
2. This relates to the design issue – what is the intervention, what is the research measuring. The Committee require clarity on the intervention/programme (even if it is a ‘preventative’ intervention) and on the elements that are research (is the intervention research or is it a programme which is being formatively evaluated?) Please elaborate in Protocol
3. Referral criteria to the programme not clear – The Committee requested clarity on this and on the process of identification, offer of service (ie can they opt out of the programme, the research or neither i.e. is it mandatory if the school says so?). Please elaborate in Protocol.
4. The Committee asked for more information/description around what is in the intervention (prevention programme), noting the peer review also raised the lack of detail as an issue. The Committee asked how the 1 hour per week will be spent, for instance does the programme begin with focus groups, if so are they age-grouped, what is the content outline that will be given to the group leader and will there be any questionnaires for participants to fill in before and after? Please elaborate in Protocol
5. The Committee also asked about the interviews. How will you choose students, what will you be asking them? The Researcher(s) explained it will be a cultural based process, explaining that the western approach has not worked in Maori. The programme would involve Maori values. The Committee stated the protocol should outline this in detail.
6. The Committee noted that the participant information sheet mentions focus groups and individual interviews.
7. The study appears to include multiple methods. Clearly this is appropriate and important to investigate the outcomes outlined, however each of these methods has different ethical issues and the committee would like further information on the method, the participants, the informed consent process for that method (including method specific information sheets) and clarity around the potential ethical issues for that method (eg for focus groups the potential risk of disclosure and confidentiality in the group, for interviews the limits of confidentiality if disclosure of risk, the management of suicidality etc. Observation and videoing especially needs to be explained further especially how this will be explained to participants. This could be done in a table or similar. It would assist if this was included in the Protocol
8. In terms of the info sheets – need to be clear:

Need school permission first (letter to school)

Need parental consent (depending on age)

Need participant consent to the specific methods being used (eg interview or focus group

1. Would be good to have a follow up point on whether participants in the programme can opt out of the research or not? Do they opt in knowing its research? If they can do the programme and not be in the research then how will the researchers manage non-participants in the focus group or observation methods?
2. For example, are the focus groups age-grouped, how will choose students to go, who chooses to go.
3. The Researcher(s) explained that at the end of day participation in the programme is up to whanau and the individual child. For instance, if the child does not think they have a problem they wouldn’t go on the programme.
4. The Committee noted the protocol has to outline how to mitigate the risks presented by this research, including aspects such as recruitment or identification of harm (e.g. suicidality, mental health crisis, self harm, harm to others) or other incidental findings (disclosure of abuse, medical conditions). The Committee acknowledged that Te Puna has experience managing these issues already, and wanted to see those management processes reflected in the Protocol and information sheets.
5. The Researcher(s) stated the school will manage the recruitment. The Committee noted that the Protocol should outline the method of selection and recruitment and what the school will be doing.
6. The Committee noted that the ethical responsibility for the safety of participants is with researchers, not the school. The Researcher(s) explained that from a Maori perspective all parties including the school and children will be involved in this process.
7. The Committee asked how the Researchers will measure whether you have met the programme objectives of improved mental health and improved well-being for rangitahi. The Researcher(s) stated face to face interview and focus groups. The Researcher(s) will ask people if it met their expectation, how. and what benefit did they have? The parents and children decide whether the outcomes are met or not. The Researcher(s) explained that these qualitative methods are good measures, and that their experience is that the feedback is honest and truthful. The Committee agreed that these outcomes are appropriate and important, but that the information about this is not written in the protocol, and the tools have not been uploaded with the application. The Committee requested further clarification of the study outcomes and the tools to measure those (related to the methods above).
8. The Committee asked what would occur in event of harm identified for child or participant. The Researcher(s) responded, indicating there would be referrals, communication out with whanau, or they can withdraw.
9. The Committee asked how researchers will obtain consent from parent/guardian of 12-15 year olds. Please provide a parent/caregiver participant information sheet and assent document for 12-15 year olds.
10. The Committee asked what kind of mitigation of stigmatisation is there. The Committee would like to see some information in the Protocol about ensuring that participation is not stigmatising. The Researcher(s) explained that whakarongo te rangatahi view is about enriching children and focusing on the strength that they have, as Maori, that this was strength and resilience based rather than deficit model of thinking. The Researcher(s) explained that if someone is said to be at risk, they are only at risk because programmes are deficit focussed. The Researchers noted the challenge with the deficient focused RFP for which this intervention successfully achieved (focus on youth ‘at risk’), whereas their intervention and research was intentionally strengths based from a positive Maori worldview. The Committee agreed this was important, and that they were supportive of the strengths focus of the programme and research to be reflected in the participant information and study documents.
11. The Committee noted the protocol (p.5) says intellectual property rights around the programme are being developed and will be discussed with the participants. Therefore, if applicable, include this in participant information sheet. The Researcher(s) confirmed that the programme was not to be sold or have a commercial focus.
12. The Committee noted that the application states data will be used for future research. The Researcher(s) stated there is no plan to re-use data, please clarify.
13. The Committee noted the HDEC application outlines the steps the Researchers plan to take if a young person's mental health gives concern. Add this detail to the protocol and information sheets.
14. Please clarify the length of the intervention – says 10 weeks in one part and 16 in another.
15. Note that health information for children needs to be kept for 10 years after they turn 16.
16. The Committee will need to review the updated participant information sheet and assent forms: <16s assent and parental consent. The Researcher(s) should consider if there is a need for separate documentation for different methods.

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

1. Key informant interview PISCF Regarding the participant information sheet for 16 years and over
2. The PIS says the school has agreed that the programme ‘will be valuable’. Amend to ‘may’.
3. Currently it says that participation is about demographic data collection. Please provide more detail on the programme (what they will be doing) eg how they will be spending the hour/week and what research they are being asked to participate in - if focus groups/interviews/ questionnaires are part of this, tell them this - advise if the sessions will be recorded.
4. Add in section on what happens if a risk is identified (referral, limits of confidentiality)
5. Add HDEC ACC statement. (HDEC form r.1.7 says treatment by a registered health practitioner will be part of the study intervention).
6. Check for duplicated sentences e.g. rights.

Consent form:

1. Remove clause about informing GP of abnormal results
2. Remove tick boxes from clauses which are non-optional for participants the PIS says consent for storing the data for future use will be obtained so add a specific clause to cover this.

Additional review from member with knowledge of Tikanga

**Participant information sheet:**

1. Pg. 2 - review statement as follows: The study has as its stated purpose ‘to investigate the impact of cultural and theoretical approaches for at risk Māori youth i.e. omit references to ‘social or health issues including mental health’.
2. Review following statement: ‘Current approval for this study has been gained as HDEC’.
3. Where ‘embarrassment’ referred to, it is suggested that the word ‘whakama’ be inserted in brackets. The same regarding Maori youth / rangatahi (consistent with practice throughout document).
4. Leave out ‘demographics which is’.
5. Remove any first person references. Change ‘I’ to ‘the lead researcher’.
6. Provide Maori Health Support details as separate and distinct form HDC Advocacy Service or the Researcher.
7. Consent Form: Suggest use of HDEC template
8. Confidentiality: Is stored on h drive sufficient and is this something participants will understand? Please reconsider.

**From the application:**

1. r.6.1: please confirm how stigmatisation will be managed. Applicant response is not detailed enough, i.e. ‘strengths based programme focussed on cultural resilience’
2. p.3.3.1: Specify type of voucher participants will receive.
3. p.4.1: Identify rangatahi ‘at risk’ demographic as starting point for potential benefits that may ensue.
4. p.4.2: whakama (embarrassment) and mana tangata (confidentiality) should have been identified as cultural issues.
5. p.4.3.1: Formal consultation is required as separate and distinct from consent.
6. On the one hand: kaupapa referred to as 'strength based', on the other, parts labelled as 'at risk and/or with social/mental health issues'.
7. By Maori for Maori kei te pai, heoi ano me aro ki te kounga (quality) including appropriateness of lead researcher. In this case it would appear that she knows or at least is familiar with these rangatahi. Is there a) a conflict, or b) potential bias. Please consider this.
8. Regarding Maori consultation, Bay of Plenty DHB has a Maori Health Runanga. Perhaps contacting their Chair a possible/acceptable option.

Decision

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

* Please provide age appropriate information sheets and assent forms for younger participants and amend the existing information sheets and assent/consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Provide further information on the study design. The Committee noted that the protocol required more detail in order to reduce risks involved in the research. The detail does not require changing the methodology, rather documenting the current plan with more detail. For example, outcome measures, recruitment, managing any incidental findings. Please view the areas that the HDEC has requested strengthening of the protocol (*Ethical Guidelines for Intervention Studies para* 5.4)

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

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| **7** | **Ethics ref:** | **18/NTA/20** |
|  | Title: | Comparison of the blood levels of two forms of tamsulosin tablets in healthy volunteers under fasting conditions |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Southern Cross Pharma Pty Ltd |
|  | Clock Start Date: | 08 February 2018 |

Dr Noelyn Hung, Dr Tak Hung ānd Mrs Linda Folland were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This is a standard bioequivalence study with a single dose and crossover design under fasting conditions.
2. The drug being assessed is a generic tamsulsocin (Southern CrossPharma) and the comparator is branded Flowmaxtra.
3. Dose 0.4mg, a standard daily dose. This is a selective alpha adrenergic receptor antagonist marketed for years for urinary flow problems due to benign prostatic hypertrophy. It has also been used off-label in women for functional urinary voiding problems as evidenced by the 2017 metaanalysis of 6 RCT involving 764 women.
4. 2 weekends at Zenith Blood tests up to 56 hours after dosing; total blood drawn over 10 days=354ml.

Summary of ethical issues (outstanding)

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

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

1. Adjust information in participant information sheet and advertisements with respect to side effects in women. While they will be spared the small risk of priapism and retrograde ejaculation, they are at risk of dizziness/ constipation/ headache etc as are men.
2. Include a sentence to explain the drug has been used off label in women for urinary flow problems, otherwise it may seem that women are being tested unnecessarily

Decision

This application was *approved* by consensus.

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| **8** | **Ethics ref:** | **18/NTA/21** |
|  | Title: | Comparison of the blood levels of two forms of tamsulosin tablets in healthy volunteers under fed conditions. |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Southern Cross Pharma Pty Ltd |
|  | Clock Start Date: | 08 February 2018 |

Dr Noelyn Hung, Dr Tak Hung ānd Mrs Linda Folland were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This is a standard bioequivalence study with a single dose and crossover design under fed conditions.
2. The drug being assessed is a generic tamsulsocin (Southern CrossPharma) and the comparator is branded Flowmaxtra.
3. Dose 0.4mg, a standard daily dose. This is a selective alpha adrenergic receptor antagonist marketed for years for urinary flow problems due to benign prostatic hypertrophy. It has also been used off-label in women for functional urinary voiding problems as evidenced by the 2017 metaanalysis of 6 RCT involving 764 women.

Summary of ethical issues (outstanding)

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

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

1. Adjust information in PISC and advertisements with respect to side effects in women. While they will be spared the small risk of priapism and retrograde ejaculation, they are at risk of dizziness/ constipation/ headache etc as are men.
2. Include a sentence to explain the drug has been used off label in women for urinary flow problems, otherwise it may seem that women are being tested unnecessarily

Decision

This application was *approved* by consensus.

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| **9** | **Ethics ref:** | **18/NTA/22** |
|  | Title: | Comparison of the blood levels of two forms of tamsulosin tablets in healthy volunteers under fasting conditions and at steady state. |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Southern Cross Pharma Pty Ltd |
|  | Clock Start Date: | 08 February 2018 |

Dr Noelyn Hung, Dr Tak Hung ānd Mrs Linda Folland were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This is a multiple dosing sister study to the prior single dosing study - reference 18/NTA/20. In this study, participants are randomised to one brand of tamsulosin 0.4mg daily for 5 days, followed by a 10 day washout, followed by the other brand of tamsulosin 0.4mg taken daily for 5 days. Participants attend Zenith every day to be dosed but are free to leave (with a free breakfast) after 30 minute. They return for an overnight stay for multiple bloods on the evening of the penultimate dosing day of each period. N=28

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 that this study involves more days, and this should be reflected in payment, as well as amount of blood drawn. Please review.
2. The Committee asked about the excipients list. The Researcher(s) stated Southern Cross should use the same one for marketing, but the researchers could not be sure.

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

1. Include a sentence to explain the drug has been used off label in women for urinary flow problems, otherwise it may seem that women are being tested unnecessarily

Decision

This application was *approved* by consensus.

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| **10** | **Ethics ref:** | **18/NTA/23** |
|  | Title: | (duplicate) REDUCCTION |
|  | Principal Investigator: | Dr David Semple |
|  | Sponsor: | The George Institute |
|  | Clock Start Date: | 08 February 2018 |

David Semple, Martin Gallagher’, A/Prof Gallagher, Dr Sradha Kotwal and Saragh Coggan were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This is an observational study of patients from 5 renal dialysis units who have a central venous catheter inserted for dialysis (N~1000) between 7/2018-10/2020.
2. Data collected is all routinely available in the medical record and will be accessed retrospectively.
3. The data of interest relates to catheter infection and will include: data collection at insertion (patient demographics, diabetes, immuno-suppressives, features related to catheter insertion), data collection during the life of the catheter about any manipulation, suturing etc, data when it is removed including reason, information on bugs etc if removed for bacteraemia
4. There will also be intermittent data linkage every 1-2 years with hospitalisation data (National Minimum Dataset) and Mortality Register.
5. This study is part of the Phase 4 of a cluster step wedged Australian intervention study in which progressively, 37 Australian renal units moved from 'usual practice' around catheter care, to protocolised care from December 2016. Units were randomised to a staggered start and the baseline data was collected while units waited in line for their turn to implement the new protocols.
6. The New Zealand data will provide further baseline data for the study which as well as swelling the 'control' data pool, will provide contemporaneous data to the Australian units which are all now in the intervention phase.
7. This application was declined in December 2016 in New Zealand when it sought to randomise New Zealand units into the intervention without individual participant consent.

Summary of ethical issues (resolved)

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

1. The researcher has made a case for a 'waiver of consent' for the retrospective use of unconsented data under NEAC Observational Guideline 6.43. The Committee accepted this justification.
2. The New Zealand data will be entered with a unique identifier, onto the Australasian database. It will also remain on the New Zealand server in an identified form until the end of the study to allow linkages to be made.
3. The Researcher(s) explained in New Zealand only standard of care data accessed.
4. The Researcher(s) noted no prospective interventions
5. The Researcher(s) noted no additional study data was being collected beyond standard of care data.
6. The Committee stated that data linkage would require an amendment to the study which must be reviewed prior to any linking being undertaken and which would require more detail about the proposed linking than has currently been provided.

Decision

This application was *approved* by consensus.

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| **11** | **Ethics ref:** | **18/NTA/24** |
|  | Title: | CPAP in Radiotherapy |
|  | Principal Investigator: | Dr Louis Lao |
|  | Sponsor: |  |
|  | Clock Start Date: | 08 February 2018 |

Ms Suzanne Lydiard 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 interventional cohort study seeks to investigate how using Continuous Positive Airways Pressure (CPAP) during radiotherapy for central lung tumours affects the movement of tumor and other mediastinal structures,quality of CT planning and whether it confers advantages such as more effective tumour treatment and/or less radiation to critical central structures.
2. The technique has been trialled on lung tumours in central and peripheral locations but not specifically in the central tumour group who potentially stand to gain the most benefit.
3. Based on image analysis and physics, the radiation oncologist will decide whether CPAP-radiotherapy may be of benefit by either moving healthy structures out of the firing line and/or allowing safe intensification of tumour dose
4. Patients are offered radiation either with or without CPAP according to the above decision.

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 written consent is taken at beginning of appointment. The Researcher(s) confirmed it was.
2. The Committee asked why entry age is 18 instead of 16. The Researcher(s) stated it related to paediatric grouping. The Committee noted that if it was beneficial to have younger participants over 16 in the study they could amend the inclusion exclusion criteria.
3. The Committee asked whether there is a conflict of interest in recruitment. The Researcher(s) explained their recruitment process, noting the mitigation of conflict by having people not involved in their care also being involved in the discussion, recruitment and consent.

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 how the sample size was determined. The Researcher(s) stated it was based on a previous study, as well as informed by a realistic calculation of number of patients who come through hospital. The Committee explained power calculations and as this seems to be a pilot study advised the researchers talk with a biostatistician.
2. The Committee stated that the researchers need to amend the protocol; this is not a non-inferiority study.
3. The Committee asked about any funding or financial reimbursement for carparks.
4. The Committee noted participant information sheet pg. 5 states data is stored for 40 years, and then 10 years after death, but also states 10 years. Please clarify between clinical vs research data, and also note that the data is de-identified, not anonymous. The Committee noted it must be made clear to participants if they researchers want to keep data for future studies. The Researcher(s) stated they would check the post-study data plans.
5. The Committee ask about long term follow up for outcomes, will this involve re-identification. The Researcher(s) explained clinical patients will have long term clinical follow up as part of standard of care. The Committee noted this should be clear, and research should not be confused with clinical practice.

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

1. If pneumothorax is a risk please make this clear.
2. Explain 'sleep apnoea' or remove reference to it
3. Offer all a lay summary of results in due course via tick box on Consent.( to themselves or relative)
4. Amend anonymised to de-identified and explain what this means.
5. Amend to state data will not be published in a form that could reasonably be expected to identify you, as per the Health Information Privacy Code.

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*).
* Provide further information on the study design, *in particular the sample size* (*Ethical Guidelines for Intervention Studies para* 5.4)
* Please see (*Ethical Guidelines for Intervention Studies para* 7.2) for more information on levels of data confidentiality.

This following information will be reviewed, and a final decision made on the application, by Mrs Rochelle Style and Dr Nora Lynch.

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| **12** | **Ethics ref:** | **18/NTA/26** |
|  | Title: | GS-US-417-4048: A Clinical Study of Filgotinib in Adults with Normal and Reduced Liver Function |
|  | Principal Investigator: | Prof Edward Gane |
|  | Sponsor: | Gilead Sciences Pty Limited |
|  | Clock Start Date: | 08 February 2018 |

Prof Edward 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 Christine Crooks declared a potential conflict of interest, and the Committee decided to have Dr Crooks remain in the room but not take part in the discussion or decision of the application.

Summary of Study

1. Filgotinib is being developed as a new treatment for patients suffering from rheumatoid arthritis including those with cirrhosis. Most drugs are broken down by the liver and cleared from the body in the bile and therefore can build up in the body of patients with damaged liver from cirrhosis from any cause.
2. This current study will determine whether the dose of filgotinib should be reduced in patients with cirrhosis. Because filgotinib is mainly broken down in the intestines and largely cleared from the body by the kidneys, significant build-up is not expected. Therefore the first cohort of patients in this hepatic impairment study will have moderately reduced liver function. If no significant build up occurs, then the next group pf patients will have severely reduced liver function. If significant build up is seen, then the next group of patients will have only mildly reduced liver function.

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 how high was the risk of male infertility. The Researcher(s) stated risk relates to doses, with this dose, the risk is low, adding that males were not excluded from a large study conducted overseas. The Researcher(s) advise participants to take or use contraception.
2. The Committee asked about compensation if partner get pregnant and the baby has harm. The Researcher(s) and The Committee noted the participant information sheet outlines what would happen in this circumstance.

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

1. The Committee noted the right to access health information, please remove limiting statements. It may be stated that accessing records would result in removal from the study, due to it being blinded, however participants retain the right to access their records.
2. HIV – make it clear that this is notifiable on pg. 4 currently does so already, on pg. 6
3. Add to the main PIS some brief wording about what would happen if a pregnancy occurs, the opportunity to participate in follow-up research and the fact that no costs will be paid for the pregnancy, delivery or care of the child. This information is currently only provided on the separate participant information sheet, which is not given until pregnancy is identified.
4. Some heading are duplicated.
5. The Committee noted some of these participants are healthy, yet the future unspecified research or broad consent mentions disease. Please revise the documentation to ensure that it is applicable to both healthy volunteers and those with a specific disease.
6. Add the address of the laboratory for the future unspecified research.
7. Please remove statements in the PIS and consent form which state that ‘no data which could identify me personally will be used in any reports on this study’ and amend to: “information will not be published in a form that could reasonably be expected to identify you”.
8. Please amend the wording under the heading “What happens if you are injured? Medical treatment and compensation for study-related injury” to include an additional paragraph to the following effect: *“The guidelines require that the compensation you receive be appropriate to the nature, severity and persistence of your injury. This means you are unlikely to receive compensation from Gilead Sciences Inc unless your injury is serious and not just temporary. You might also not receive compensation from Gilead Sciences Inc if your injury was caused by the investigators, if there is a deviation from the proposed plan of research, or if your injury was caused solely buy you. If you are injured as a result of the trial, but your injury was caused by the investigators (or the institution/hospital where the trial took place) or as a result of a deviation from the proposed plan of research, you will not be covered by ACC and may have to pursue a civil action against the investigators (or institution). Ethics Committees in New Zealand require that Researcher(s) and their institutions have indemnity cover for such risk and the sponsor for this research also provides insurance cover. Both may be subject to exclusions and limitations which preclude a payout*.

Decision

This application was *approved* by consensus with non-standard conditions.

## General business

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

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| **Meeting date:** | 20 March 2018, 08:00 AM |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

The following members tendered apologies for this meeting.

1. **Problem with Last Minutes**

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

The meeting closed at 6.20pm