

22 July 2016

Mrs Tanith Alexander

Dear Mrs Alexander

Re: Ethics ref:	16/NTA/90
Study title:	Different Approaches to MOderate- and late-preterm Nutrition: Determinants of feed tolerance, body composition and development

I am pleased to advise that this application has been approved by the Northern A Health and Disability Ethics Committee. This decision was made through the HDEC-Full Review pathway.

Summary of Study

1. The study investigates whether the nutritional approach taken a few days after birth in moderate pre term babies has long-term impacts on mental and metabolic health. The study aims to improve outcomes for babies.
2. The Researcher(s) explained that the babies are born between 32 and 36 weeks gestation, only a few weeks early. The standard of care is to try and establish breast milk feeding with the aim to have only have breast milk by the time they go home. However, it takes time for babies to start feeding on breast milk, sometimes several days though it could be up to a week or more. This is for a variety of reasons – primarily related to the immaturity of the babies. Their gut may not be developed so they can't tolerate milk, or they have not developed sucking mechanisms that can manage swallowing and breathing, or risks of aspirating milk into their lungs. Until the babies are ready they need some form of supplementary feeding, and the method of early feeding is in equipoise among both New Zealand clinicians and international guidelines.
3. The Researcher(s) explained that some consultants use a 10% dextrose that is rubbed into the gums of babies, others use intravenous nutrition and others use breast milk or a milk formula.
4. Researchers explained the approach to nutritional feeding for preterm babies varied between consultants. It is not known what the optimum approach is.

Summary of ethical issues (resolved)

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

5. The Committee queried if babies are assigned to arms of the study or whether consultants choose and the study data is only observed. The Researcher(s) stated randomisation occurs to avoid bias in study results.

6. The Committee queried whether there are any babies who don't get treatment in this study. The Researcher(s) stated all babies get one of the treatments in equipoise, and if a certain type of treatment is determined to be clinically required the baby would not be randomised, but they would inevitably get one of the three types of nutrition in this study.
7. The Researcher(s) added they are also adding smell and taste to those having IV treatment feeding, as a sub study, by breast milk being added to cotton buds and wiped on the baby's face and nose prior to feed.
8. The Researcher(s) confirmed no samples sent overseas. Samples are stool and saliva.
9. Confirmed no samples stored beyond duration of study.
10. The Committee queried the consenting process, noting the acute context. The Researcher(s) stated they will try in all cases to speak to mothers before they go into labour, adding some potential participants can give consent before labour due to pre-admission.
11. The Researcher(s) explained that there was a cohort who delivers very quickly, as they come into hospital and are directed straight to the delivery suite. The Researcher(s) felt it was not appropriate to talk to this group before delivery, however they will seek consent after their baby had been born. In these cases families are given time to discuss with family or whanau. This period is about 24 hours. The Researcher(s) then come back to the family and seek their consent. Anecdotally, this method works effectively, and balances respect for the family as well as the acute nature of feeding.
12. The Researcher(s) noted it was important not to exclude this group of women, whose babies may have particular feeding needs.
13. The Committee queried if there was a potential conflict of interest if the individual's treating physician was also the recruiting researcher. The Researcher(s) stated often the recruiting individual was a clinical fellow or part of the research team, though acknowledged it could be an attending consultant on occasion, though past experience suggests the conflict is managed as they will not approach if there is a medical reason not to recruit, and that participation is voluntary and the arms are in equipoise.
14. The Researcher(s) explain other studies have reviewed the consenting process used in this study and none of the respondents have raised a problem with the proposed process (in particular of those who decline).
15. The Committee asked about Maori children who are preterm, in terms of prevalence. The Researcher(s) stated that Maori experience an increase of preterm babies at about 0.5 percent compared to non-Maori.
16. The Researcher(s) stated they consult with Maori research advisor at ADHB and Waitemata, as well as with Auckland University. The Researcher(s) explained that they have Maori research nurses who both help with recruitment as well as playing a big part in the follow up phase. The Researcher(s) added prior research experience in this context show no difference in recruitment rates between ethnicities.

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

17. The Committee noted that it is not very clear in participant documentation that there are 8 factor groups - maybe add a table (like the one in the protocol) or some better explanation of this for participants.
18. The Committee noted that the Health Research Council reviewers noted that maternal environment doesn't seem to have been included in measures as a confounder, and asked about the collection of health information collected. The Researcher(s) stated they are looking at these variables. The Committee

requested that if health information was to be used it should be clearly stated in the Participant Information Sheet.

19. Remove non-optional yes or no statements from the consent form.
20. Needs a bit more info on the tests on the sample, where samples are kept (ie going overseas?) and how long for.

Conditions of HDEC approval

HDEC approval for this study is subject to the following conditions being met prior to the commencement of the study in New Zealand. It is your responsibility, and that of the study's sponsor, to ensure that these conditions are met. No further review by the Northern A Health and Disability Ethics Committee is required.

Standard conditions:

1. Before the study commences at *any* locality in New Zealand, all relevant regulatory approvals must be obtained.
2. Before the study commences at *any* locality in New Zealand, it must be registered in a clinical trials registry. This should be a WHO-approved (such as the Australia New Zealand Clinical Trials Registry, www.anzctr.org.au). However <https://clinicaltrials.gov/> is acceptable provided registration occurs prior to the study commencing at *any* locality in New Zealand.
3. Before the study commences at a *given* locality in New Zealand, it must be authorised by that locality in Online Forms. Locality authorisation confirms that the locality is suitable for the safe and effective conduct of the study, and that local research governance issues have been addressed.

Non-standard conditions:

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

The Committee noted that it is not very clear in participant documentation that there are 8 factor groups - maybe add a table (like the one in the protocol) or some better explanation of this for participants.

The Committee noted that the Health Research Council reviewers noted that maternal environment doesn't seem to have been included in measures as a confounder, and asked about the collection of health information collected.

The Researcher(s) stated they are looking at these variables. The Committee requested that if health information was to be used it should be clearly stated in the Participant Information Sheet.

Remove non-optional yes or no statements from the consent form.

Needs a bit more info on the tests on the sample, where samples are kept (ie going overseas?) and how long for.

Non-standard conditions must be completed before commencing your study. Non-standard conditions do not need to be submitted to or reviewed by HDEC before commencing your study.

If you would like an acknowledgement of completion of your non-standard conditions letter you may submit a post approval form amendment. Please clearly identify in the amendment that the changes relate to non-standard conditions and ensure that supporting documents (if requested) are tracked/highlighted with changes.

For information on non-standard conditions please see section 128 and 129 of the Standard Operating Procedures at <http://ethics.health.govt.nz/home>.

After HDEC review

Please refer to the *Standard Operating Procedures for Health and Disability Ethics Committees* (available on www.ethics.health.govt.nz) for HDEC requirements relating to amendments and other post-approval processes.

Your next progress report is due by 21 July 2017.

Participant access to ACC

The Northern A Health and Disability Ethics Committee is satisfied that your study is not a clinical trial that is to be conducted principally for the benefit of the manufacturer or distributor of the medicine or item being trialled. Participants injured as a result of treatment received as part of your study may therefore be eligible for publicly-funded compensation through the Accident Compensation Corporation (ACC).

Please don't hesitate to contact the HDEC secretariat for further information. We wish you all the best for your study.

Yours sincerely,

A handwritten signature in black ink, appearing to read 'B J Fergus', with a horizontal line underneath.

Dr Brian Fergus
Chairperson
Northern A Health and Disability Ethics Committee

Encl: appendix A: documents submitted
appendix B: statement of compliance and list of members

Appendix A
Documents submitted

<i>Document</i>	<i>Version</i>	<i>Date</i>
Evidence of scientific review: HRC scientific review	1	14 June 2016
CVs for other Investigators: Professor Frank Bloomfield CV	1	16 June 2016
CVs for other Investigators: Dr Jane Alsweiler	1	16 June 2016
Survey/questionnaire: Breastfeeding survey	1	16 June 2016
CV for CI: Tanith Alexander CV	1	16 June 2016
PIS/CF: PIS	1	16 June 2016
PIS/CF: CF	1	16 June 2016
Protocol: Research protocol	1	16 June 2016
CVs for other Investigators: Dr Michael Meyer CV	1	16 June 2016
Covering Letter: Cover letter	1	20 June 2016
PIS/CF for persons interested in welfare of non-consenting participant: Information sheet	1	21 June 2016
PIS/CF for persons interested in welfare of non-consenting participant: Consent form	1	21 June 2016

Appendix B Statement of compliance and list of members

Statement of compliance

The Northern A Health and Disability Ethics Committee:

- is constituted in accordance with its Terms of Reference
- operates in accordance with the *Standard Operating Procedures for Health and Disability Ethics Committees*, and with the principles of international good clinical practice (GCP)
- is approved by the Health Research Council of New Zealand's Ethics Committee for the purposes of section 25(1)(c) of the Health Research Council Act 1990
- is registered (number 00008714) with the US Department of Health and Human Services' Office for Human Research Protection (OHRP).

List of members

<i>Name</i>	<i>Category</i>	<i>Appointed</i>	<i>Term Expires</i>	<i>Present on 12/07/2016?</i>	<i>Declaration of interest?</i>
Dr Brian Fergus	Lay (consumer/community perspectives)	11/11/2015	11/11/2018	Yes	No
Ms Rosemary Abbott	Lay (the law)	15/03/2016	15/03/2019	Yes	No
Dr Karen Bartholomew	Non-lay (intervention studies)	13/05/2016	13/05/2019	Yes	No
Dr Charis Brown	Non-lay (intervention studies)	11/11/2015	11/11/2018	Yes	No
Ms Susan Buckland	Lay (consumer/community perspectives)	11/11/2015	11/11/2016	Yes	No
Ms Shamim Chagani	Non-lay (health/disability service provision)	11/11/2015	11/11/2016	Yes	No
Dr Christine Crooks	Non-lay (intervention studies)	11/11/2015	11/11/2018	Yes	No
Dr Kate Parker	Non-lay (observational studies)	11/11/2015	11/11/2018	No	No

Unless members resign, vacate or are removed from their office, every member of HDEC shall continue in office until their successor comes into office (HDEC Terms of Reference)

<http://www.ethics.health.govt.nz>