Health and Disability Ethics Committees
Ministry of Health
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18 December 2017

Mr Ben Warren
Department of Psychology
University of Canterbury
Private Bag 4800
Christchurch 8140

Dear Mr Warren

Re:	**Ethics ref:**	**17/STH/241**
	Study title:	Anxiety and micronutrients: A double blind, randomised controlled trial with Zinc and Vitamin B6

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

Summary of Study

1. The study is a double blind, randomised controlled trial that investigates if Zinc and Vitamin B6 improve symptoms of anxiety and depression.

Summary of ethical issues (resolved)

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

2. The Committee asked whether the coordinating investigator wouldcommercially benefit from the study. The CI confirmed that he was the owner of a vitamin supply business but that the doses of the products used in the current study were such that he would not be able to supply them commercially should benefit be shown.
3. The Committee were satisfied that this project is not a commercially-sponsored intervention study and that participants will be eligible to apply for ACC compensation if necessary.
4. The committee queried the scientific purpose of the open label component of the study. The researcher confirmed that all scientific outcome measures (efficacy and safety) would be based only on the randomised component of the study. The researcher confirmed that the open-label component of the study was purely an incentive to increase recruitment.
5. The committee questioned whether a cross-over design would be more useful scientifically than the inclusion of an open-label phase. The researcher stated this would not be possible as the wash-out period for zinc and B6 was not known. Further, it was not possible to assess washout based on blood or urine zinc / B6 concentrations due to homeostasis. The committee questioned whether an arbitrary period of 6 weeks would suffice, given that was the period selected to assess efficacy and safety. The researcher stated that this would not be possible.
6. The Committee queried the purpose of the naturalistic follow-up. The Researcher explained that it is to explore if participants have made lifestyle changes following

study participation and if there have been any continued benefits. The committee noted that the study design would confound these results, as would the aspect of self-selection of the follow-up group, and expressed reservations about the scientific validity of such follow-up.

7. The Committee asked for the makeup of the data safety monitoring committee. The Researcher explained that the group is made up of the study clinicians and the supervisor for the Researcher's PHD. The Committee asked that an external reviewer be added to this group.
8. The Committee queried how recruitment would occur. The Researcher explained recruitment would be at a national level via a network of GP's who are interested in the topic. Advertising would be used if there were low numbers of participants.
9. The Committee asked what would happen if participants experienced a deterioration of their symptoms during the study. The Researcher explained that they would be referred onto the study clinician who is a psychiatrist as well as their GP.
10. The Committee stated that participants should be invited to a centre to discuss the project and to seek consent. If this is not possible (ie due to distance) then there should be a phone discussion and an information sheet and consent form mailed to them. The study must be discussed in detail over the phone, an opportunity must be provided to discuss any questions about study participation, and the participant must be given time to discuss with others prior to giving consent. All consent must be evidenced.
11. The researchers noted that the doses used in the study required a doctor's prescription. If a participant wished to continue with zinc and B6 after the active component of the study was completed, the researchers would inform the participant's GP regarding prescription details.

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

12. Remove tick boxes from the consent form for all items that are not truly optional.

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 Southern 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:

- Please amend the information sheet and consent form, taking into account the suggestions made by the Committee.
- As the doses used during the study require prescription, please ensure prescriptions are made and dispensed in accordance with all legal requirements.

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.

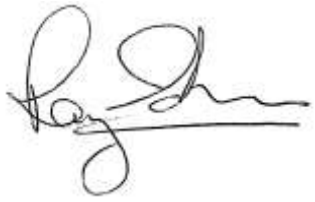
Your next progress report is due by 17 December 2018.

Participant access to ACC

The Southern 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,



Ms Raewyn Idoine
Chairperson
Southern Health and Disability Ethics Committee

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

Appendix A
Documents submitted

Document	*Version*	*Date*
CV for CI: Personal CV for Ben Warren	1	22 November 2017
Survey/questionnaire: (Screening) Medical History Questionnaire	1	22 November 2017
Evidence of scientific review: Evidence of review from academic staff	Gini/Julia	22 November 2017
PIS/CF: Information sheet & consent form for participants	1	23 November 2017
Maori Consultation Approval	1	23 November 2017
Advertisement copy for facebook and social medida	facebook advertiseme nt	23 November 2017
CVs for other Investigators: Julia Rucklidge Full CV	1	21 November 2017
CVs for other Investigators: Roger Mulder Full CV	1	21 November 2017
Survey/questionnaire: (Safety Outcome) Adverse events & Side Effects Checklist	1	21 November 2017
Survey/questionnaire: (Secondary Outcome) Depression, Anxiety and Stress scale	(Lovibond & Lovibond, 1995)	21 November 2017
Survey/questionnaire: (Secondary Outcome) Eating Behaviours Questionnaire	(Baker, Little, & Brownell, 2003)	21 November 2017
Survey/questionnaire: (Primary Outcome) General Anxiety Disorder	(Spitzer, Kroenke, Williams, & Löwe, 2006)	21 November 2017
Survey/questionnaire: (Primary Outcome) Modified Clinical Global Impressions	(Spearing, Post, Leverich, Brandt, & Nolen, 1997)	21 November 2017
Survey/questionnaire: (Secondary Outcome) Profile of Mood States scale	(Curran, Andrykowski, & Studts, 1995)	21 November 2017
Survey/questionnaire: (Secondary Outcome) Practitioner Pyrroles Screening Questionnaire	(Larson, 2011)	21 November 2017
Survey/questionnaire: (Secondary Outcome) Walsh/Jaa Pyroluria Questionnaire	(Walsh & Jaa, 2017)	21 November 2017
Survey/questionnaire: (Secondary Outcome) Quality of Life Scale	(Burckhardt & Anderson, 2003)	21 November 2017
Survey/questionnaire: (Secondary Outcome) Social Phobia and Anxiety Inventory	(de Vente, Majdandžić, Voncken, Beidel, & Bögels,	21 November 2017
Survey/questionnaire: (Additional Outcomes) Treatment Satisfaction Questionnaire	(Atkinson et al., 2004)	21 November 2017
Protocol: Protocol for anxiety and micronutrients	1	22 November 2017
Application		
Evidence of scientific review: Additional to SCOTT review	1	24 November 2017

Appendix B
Statement of compliance and list of members

Statement of compliance

The Southern 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 00008713) with the US Department of Health and Human Services' Office for Human Research Protection (OHRP).

List of members

Name	*Category*	*Appointed*	*Term Expires*	*Present on 05/12/2017?*	*Declaration of interest?*
Ms Raewyn Idoine	Lay (consumer/community perspectives)	27/10/2015	27/10/2018	Yes	No
Dr Sarah Gunningham	Non-lay (intervention studies)	27/10/2015	27/10/2018	Yes	No
Assc Prof Mira Harrison-Woolrych	Non-lay (intervention studies)	27/10/2015	27/10/2018	Yes	No
Dr Fiona McCrimmon	Lay (the law)	27/10/2015	27/10/2018	Yes	No
Dr Anna Paris	Lay (other)	24/08/2017	24/08/2020	Yes	No
Dr Nicola Swain	Non-lay (observational studies)	27/10/2015	27/10/2018	No	No
Dr Devonie Waaka	Non-lay (intervention studies)	13/05/2016	13/05/2019	Yes	No
Dr Mathew Zacharias	Non-lay (health/disability service provision)	27/10/2015	27/10/2018	Yes	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