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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 17 April 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 20 March 2018 |
| 1.30pm | New applications (see over for details) |
| 1.30-1.55  1.55-2.20  2.20-2.45  2.45-3.10  3.10-3.35  3.35-4.00  4.00-4.25  4.25-4.50 | i 18/NTA/44  ii 18/NTA/48  iii 18/NTA/49  iv 18/NTA/50  v 18/NTA/53  vi 18/NTA/57  viii 18/NTA/59  vii 18/NTA/58 |
| 5.00pm | General business:   * Noting section of agenda |
| 5.15pm | 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 |
| Dr Kate Parker | Non-lay (observational studies) | 11/11/2015 | 11/11/2018 | Apologies |
| 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 the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

## Confirmation of previous minutes

The minutes of the meeting of 20 March 2018 were confirmed. It was noted that the start time of the 17 April 2018 should be 1:00pm.

## New applications

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| **1** | **Ethics ref:** | **18/NTA/44** |
|  | Title: | Medication use and breast cancer outcomes |
|  | Principal Investigator: | Professor Mark Elwood |
|  | Sponsor: |  |
|  | Clock Start Date: | 14 March 2018 |

Professor Mark Elwood and Dr Sandar TinTin were present in person for discussion of this application.

Potential conflicts of interest

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

Dr Karen Bartholomew declared a potential conflict of interest, and the Committee decided to have Dr Bartholomew remain in the room but not lead on the review of the application but she could take part in the discussion.

Summary of Study

1. This study aims to examine the association between the use of cardiovascular medications and cancer outcomes in New Zealand, focusing on patients with breast cancer.
2. The study will take the form of a retrospective cohort study of about 16,000 women with newly diagnosed breast cancer between 1 January 2000 and 30 June 2014 recorded in the Auckland and Waikato breast cancer registries.
3. Patient data which has been collected for a HRC funded project, will be linked to pharmaceutical data, hospital discharge data and mortality data to get updated information on the use of cardiovascular medications, comorbidities and deaths.

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 the Researchers will decide which patients to include in the study. The Researchers noted that data from all patients within a defined time period will be included to ensure a full linkage to ensure an unbiased sample.
2. The Committee queried whether approval had been sought from the individual governance bodies for the two registries. The Researcher confirmed that representatives from these registries will be co-investigators and approval had been sought.
3. The Committee noted that that the aims of the study is to estimate the prevalence of commonly used cardiovascular medications in cancer patients and to examine their associations with cancer outcomes in New Zealand, focusing on patients with breast cancer. The Committee questioned if the hypothesis is that those cardiovascular medicines provide some unknown protection for breast cancer separate from what they would provide for heart disease. The Researcher clarified that it could be protection or detriment.
4. The Committee queried whether the Researcher will adjust for differences between ethnic groups, particularly as management of increased cardiovascular risk is not equally distributed across the population for Māori and Pacific in the Auckland region. The Researcher confirmed that will be able to subdivide and look at Māori and Pacific people specifically to examine whether there is an effect between groups.
5. The Committee queried if the Researcher will know why people are on the medicines. The Researcher noted that they will have hospital and co-morbidity data but won’t have a direct statement as to why a certain individual has been put on a medicine. The Committee suggested linking to predict as this would have the risk assessment scores. The Researcher noted that they explored linking to Predict and linking to IDI but appears quite complex at this stage.
6. The Committee queried if the co-investigators from the registries are breast cancer physicians. The Researcher noted that this study is being done within an umbrella of studies relating to breast cancer. A clinical group meet 2-3 times a year via teleconference and this includes a leading breast cancer surgeon, other surgeons, medical oncologists, and have access to a pathologist, if required. The Researcher confirmed that there are good clinical links in place and discussions take place regularly.

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 queried what data is being linked, where the linking is being done and the security arrangements around this. The Researcher confirmed that the basic data they will start with is the 2 main breast cancer registries at Waikato and Auckland. These collect data from freshly diagnosed breast cancer patients and are linked to the hospital patient record system. The process to collect this data has already been through the ethical review process. The Researcher noted that they will analyse this data. That data contains identifiable data which the Researcher does not require, but will include NHI numbers. The Researcher is suggesting that they link that data to a whole range of data held centrally e.g., discharge data, mortality data. The Researcher noted that the linkage will be done by the Ministry of Health. The Researcher would provide the NHI numbers of the patients they wish to obtain further information on to the Ministry of Health and the linkage would be carried out within the Ministry of Health and then returned to the Researcher with the NHI numbers, with the linked data but no other identifiable information. The Committee requested that more detail is included in the protocol to better explain where the data linkage is being done, by whom, data governance arrangements, the time period, and that de-identified information is being returned.
2. The Committee noted that the protocol refers to other cancers and potential use of Integrated Data Infrastructure (IDI). The Researcher noted that this application is specific to breast cancer but were exploring the potential to look at other cancers as a separate study. Please ensure it is clear in the protocol that this study is specific to breast cancer.

Decision

This application was *approved* *with a non-standard condition* by consensus. The non-standard condition for this study is:

* Please amend the protocol to include detail on where the data linkage is being done, by whom the time period, the data governance arrangements, and that de-identified information is being returned.

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| **2** | **Ethics ref:** | **18/NTA/48** |
|  | Title: | Smart Search |
|  | Principal Investigator: | Dr Yiwen Zhang |
|  | Sponsor: | Orion Health |
|  | Clock Start Date: | 27 March 2018 |

Dr Yiwen Zhang and Dr Kelly Atkinson were present in person for discussion of this application.

Potential conflicts of interest

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

Dr Karen Bartholomew declared a potential conflict of interest, and the Committee decided to have Dr Bartholomew remain in the room but not take part in the discussion or the decision whether to approve or decline the research.

Summary of Study

1. This research aims to develop novel tools for improving access to the large volume of healthcare data that is unstructured, and therefore currently impervious to searching and effective information retrieval.
2. This research will involve:

* Review of Waitemata District Health Board (WDHB) clinical documents by two WDHB ICU clinicians, where each clinician will manually annotate (tag) text inside each document which they believe is relevant to their work.
* Transferring annotated clinical data to a secure, access-controlled research area within Orion Health - this room is designed to be a secure, encrypted environment specifically for research using identifiable personal health information, similar in setup to Statistics New Zealand's Integrated Data Infrastructure (IDI) access points.
* Using machine learning to produce a predictive model which can accurately identify text related to ICU clinicians from within document text, resulting in a proof of concept search app.
* The two WDHB ICU clinicians evaluating the performance of this app to make sure its search works as anticipated.

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 if research designing an app to search medical text had been carried out elsewhere in the world. The Researcher noted that it had but was the first time in New Zealand. The Committee queried why the study was being carried out again as the tool was already available overseas. The Researcher clarified that they want the data to be more relevant to a New Zealand context.
2. The Committee queried at what stage the data is deleted if a successful model is developed. The Researcher noted that clinical data would be deleted after 3 years but the model would be kept indefinitely because protected health information cannot be extracted from the model.
3. The Committee noted for future information when a study purpose claims a health benefit then the CI should be a clinician.

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 requested detail on the WDHB data bank governance procedures. The Researcher noted that Orion Health have a policy in place. Please include details in the protocol around data governance policy at Orion Health and WDHB.
2. The Committee queried the type of information that is coming from WDHB. The Researcher noted that this would include clinical letters and discharge summaries in electronic form and not hand written notes. Please add to the protocol the type of information and other data such as electronic medicines recordings etc. that is being used in the research and improve the definition of the scope of the data being accessed. The scope and limitations of the research should clarify that hand written notes are not included. The Committee noted that the amount of data accessed should be the minimum required for the research.
3. The Committee noted that at least 15 people will have access to identifiable health information (including clinicians, data scientists, back-end engineers and front-end developers). The Committee also noted that the identifiable health information is being accessed and reviewed, not for clinical care, but for research purposes which is a secondary and unconsented use of clinical data. Please reconsider if it is necessary for all these people to have access to the identifiable health information. If so, the Committee would recommend that you maintain a log of all these people and evidence that they have signed a confidentiality agreement. Access to medical or other records for the purposes of observational studies should be restricted to appropriately qualified investigators and study associates responsible to them (Ethical Guidelines *for Observational Studies* paragraph 6.38).
4. The Committee noted that the protocol refers to de-identification of the data before delivery to external parties being managed by the published Application Programming Interface (API) so that the required level of privacy is maintained. Please provide more information around which API standards and guidelines will be used.
5. The Committee noted that the group they are targeting is a small defined group (ICU patients) and it would be easy to identify participants. The Committee requested more detail around confidentiality procedures to protect participants. The Researcher noted that data would be stored at Orion Health in a restricted access room (data bank) with no network access. Data would be transferred from the WDHB using a secure transfer or an encrypted USB drive and then content is deleted. Please ensure more information on data management and confidentiality is included in the protocol. Investigators should arrange to protect the confidentiality of such data by, for example, omitting information that might lead to the identification of individual participants, or limiting access to the data, or by other means (*Ethical Guidelines for Observational Studies* paragraph 8.2).
6. The Committee noted that a lot of information may be missed through hand written notes and that New Zealand does not have adequate electronic health records. The Committee would like more information as to how information generated from this study will be used in the future to benefit patients. The study is using a lot of identifiable data and it important that the value and merits of this are presented.
7. The protocol addresses some Maori issues but we suggest that the group engages in formal discussions with the appropriate Maori review group and advise us if any issues around the use of data relating to Maori have arisen from this review/ discussion, and incorporate any such changes in the Protocol.
8. The Committee would like more information on the purpose and real benefits associated with the project. The investigator must show how safeguards will be maintained to protect confidentiality, and that the study has the goal of protecting or advancing health (*Ethical Guidelines for Observational Studies* paragraph 6.46).
9. Peer review - the application notes that as part of the funding for the research peer review has been conducted.  The Committee requested to have a copy of the peer review.

Decision

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

* Please include more information in the protocol on data management, governance and confidentiality as detailed above.
* Please respond to the outstanding ethical concerns detailed above.

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

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| **3** | **Ethics ref:** | **18/NTA/49** |
|  | Title: | Oral administration of maternal bacteria in twins born by C-section |
|  | Principal Investigator: | Prof Wayne Cutfield |
|  | Sponsor: | University of Auckland |
|  | Clock Start Date: | 05 April 2018 |

Valentina Chiavaroli was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The aim of the study is to perform a proof-of-concept RCT to assess whether oral administration of maternal vaginal microbiota in twins born by caesarean section (CS will: (i) increase the prevalence of Bacteroides spp. and Bifidobacterium spp.; and (ii) change the bacterial population structure.
2. The project consists of two phases:
   * Phase 1: To ensure that the gauze incubated in the maternal vagina contains vaginal bacteria and to determine the viability of these bacteria.
   * Phase 2: To determine whether twins receiving the maternal vaginal microbiota have different gut bacterial strains compared to twins receiving placebo, with treated twins more closely resembling the bacterial strains of singletons vaginally-delivered.

Summary of ethical issues (resolved)

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

1. The Committee queried whether there would be infection screening in all of the cohorts. The Researcher clarified that this would be done in the women carrying twins only.
2. The Committee queried who would be doing the screening tests. The Researcher confirmed that the lead maternity carer would do this. The Committee noted that all research required tests should be carried out by the Researcher if not carried out by the lead maternity carer. The Researcher should ask for access to routine collected results.
3. The Committee queried if education level information collected in the questionnaire is relevant to the outcome of the study. The Researcher confirmed that education level is one of the variables which they may need to adjust for.

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 received an Explorer grant from the HRC which meant it was peer reviewed. Please provide a copy of the peer review.
2. Questionnaire - The Committee noted that the ethnicity question asked in the demographics questionnaire is incorrect. Please use the Health and Disability Ethnicity Data Protocols standard ethnicity collection question the when collecting ethnicity data to ensure the options available are suitable for New Zealand participants. These classifications are: New Zealand European, Māori, Samoan, Cook Islands Maori, Tongan, Niuean, Chinese, Indian, Other (such as Dutch, Japanese, Tokelauan), Please state:
3. The Committee noted that in phase 1 of the study a vaginal swab will be taken and queried what the likelihood is of identifying an illness (e.g. chlamydia) that would need to be treated. The Researcher noted that they won’t look for this bacteria but will ensure that the women are not carrying any pathogens. The Lead Maternity Carer will be asked what tests have been carried out to make sure the women are negative. The Committee noted that 40% of Auckland women are not tested for STIs and therefore to be sure that these women are not infected then screening would need to be part of the study procedure.

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

1. The brochures need amendment – they do not mention all aspects of participation, particularly the food and exercise diary and that the mother’s height and weight will be recorded and the baby will be scanned.
2. The heading ‘what else will participation in the study involve’ under the heading ‘maternal and infant questionnaire’ in the two PIS’ for Phase 2 of the research is slightly misleading because the questionnaires also include food and exercise diaries. The diaries should be split out as a separate bullet point because they are a significant component of participation, more than 15 min, and probably the most burdensome.
3. The Committee noted that the under the heading “Purpose of the study” in all three the Participant Information Sheet it states that “Children born by C-section have an increased risk of obesity and immune disorders (for example asthma and allergies)” and queried the strength of that risk. The Researcher explained that it is a modest risk in observational studies. The Committee suggested that the wording in the Participant Information Sheet is slightly overstated given the modest evidence and would prefer softer language.
4. The description of the research in all three Participant Information Sheets study title (“You and your baby are invited to take part in a study called maternal bacteria to correct abnormal gut microbiota in babies born by C-section”) suggests that there is a problem to be fixed. Please change to something less presumptive of an outcome. Similarly, with the brochures.
5. Please avoid use of the term “tummy bug” as the New Zealand population may associate that with an infection.
6. Please state in the Participant Information Sheet what would happen to a participant in the vaginal cohort if they have a C-Section. Please also note that, under the heading “What else will participation in the study involve?” in the PIS for the vaginal singleton cohort, the following statement is made: “Participation involves one clinical evaluation for you while in the hospital maternity ward for the scheduled C-section …. “whereas participants in this cohort may not have a C-section. Please amend.
7. Please ensure all three Participant Information Sheets state that study is for a PhD.
8. Data management – please include in all three how long data will be kept for. Please ensure that the Participant Information Sheet says data will be kept for 26 years for the babies and 10 years for the mothers. Please also include information about whether data collected will continue to be used subsequent to withdrawal (this is referred to in the consent form but it is not discussed in the PIS), whether data will be used for future research and rights of correction.
9. The Committee noted that the Participant Information Sheet for Phase 1 and for the C-section twins cohort in Phase 2 should not provide a guarantee that the maternal vaginal swab procedure is painless and suggested stating that there may be some discomfort.
10. The Committee queried if there will be any long term follow up over the next few years. The Researcher noted that the study is a proof of concept study at this stage and they are in the process of securing extra funding in order to follow up children to the age of 5 years. The Committee suggested adding this information to the Participant Information Sheet and seeking consent to potential follow-up.
11. The Committee requested the compensation wording is updated for accuracy, they suggested the following statement: *“If you were injured in this study, which is unlikely, you would be eligible* ***to apply*** *for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery. If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.”*
12. The Committee asked for clarity around collection of tissue as there is conflicting information in the Participant Information Sheet and application. Please review and ensure this information is consistent.
13. In the Participant Information Sheet for the C-section twins cohort under the heading “What are the possible benefits and risks of this study?”– Please remove the word “eliminate” in the sentence “To eliminate the risks of transmission of infections … “and replace with wording which refers to the reduction or management of such risks.
14. In the two PIS for Phase 2, please do not overstate the benefits of the study as this study may have little / no benefit to the mother or baby. Please also remove the sentence “In addition, you will receive valuable information on your and your babies’ health”.
15. Please include in both PIS’ for Phase 2 some brief information about what you are testing for in the infants’ stools and what tests are being performed.
16. The Committee noted that information is also being collected on the father for both Phases of the research and queried if the father had provided consent on this information being collected. Please ensure there is a consent form for the father. The Committee also queried whether it is relevant that the father is the biological father of the child. Please consider who is relevant and collect information on those people only.
17. Please ensure the Phase 2 Participant Information Sheet’ make it clear that there may be a chance that mothers cannot take part in the study even after they have passed the screening tests (for example, if they deliver early, delivery vaginally etc.).
18. In the Participant Information Sheet for twins – there are a number of diseases mentioned that are notifiable (HIV, hepatitis, gonorrhoea) and it needs to be clear that these would be notified to a Medical Officer of Health if positive.
19. The 2nd paragraph under the “risks/benefits’ section of the Participant Information Sheet needs to be moved to the section which describes what the study will involve as it include procedural related information.
20. Please review all Participant Information Sheets’ to remove typos.
21. This Participant Information Sheets’ refer to the possibility of participants asking for the return of tissue and samples such as stools. Please include this option in all consent forms.

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* paragraph *6.22*).
* Please respond to the outstanding ethical concerns detailed above.

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

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| **4** | **Ethics ref:** | **18/NTA/50** |
|  | Title: | Dementia-friendly book groups at the Care Home: Can quality of life be improved? |
|  | Principal Investigator: | Dr Dalice Sim |
|  | Sponsor: | Bupa Care NEW ZEALAND |
|  | Clock Start Date: | 05 April 2018 |

Dr Dalice Sim and Dr Brenda Sally Rimkeit 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. The aim of the study is to complete a multicentre, international RCT to test whether twice weekly, seven week book club attendance by Persons Living With Dementia (PLWD) (mild-moderate), compared to control (activities as usual at the Residential Aged Care Facility (RACF) improve quality of life.
2. The primary outcome measure is change in quality of life pre­ and post­ trial. Secondary outcome measures are changes in thriving at the RACF, Theory of Mind, cognition, mood and behaviour. Book group participants will be stratified by their level of placement at the RACF, either in rest home or hospital care, or at a secure dementia unit. Book groups will use materials adapted for people with dementia and a facilitator's manual prepared by the study authors.

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 the necessity for a participant/carer dyad and why a carer is giving information on a participant’s quality of life when the participant can give this information themselves. The Researcher confirmed that this is to seek the carer’s views on the quality of life and is an additional piece of information to use as a matched variable: carer’s views against participant’s views of quality of life. Other international studies have utilised this method.
2. The Committee queried if a participant will choose who the carer is who answers quality of life and other questions. The Researcher confirmed that this would be part of the consenting process. The Committee suggested the PLWD consent form include a section which records the name of the carer that the PLW has agreed may answer questions about him/her.

Summary of ethical issues (outstanding)

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

1. Recruitment process – The application mentions Bupa advertisements in rest homes and InterRAI screening. The Committee queried how recruitment will be done. The Researcher confirmed that Bupa staff will screen potential participants using InterRAI information from existing assessments, to avoid raising expectations if a person is not eligible to participate in the study. The Committee suggested amending the wording on the posters so that it is clear only eligible participants will be invited to participate.
2. The Committee queried if participants get to keep the books after the study. The Researcher confirmed that the RACF would keep the books. Books are only read at the book group and not taken away. Please consider if participants can take the books away with them.
3. The Committee queried if the audiotapes will be destroyed. The Researcher noted that there will be no audio recording in the study and will remove this from the study documentation.
4. Please include more information on data management in the protocol. Investigators are required to ensure the adequate physical and electronic security of data (*Ethical Guidelines for Observational Studies* paragraph 8.3).

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

1. Please include more information on data management in the Participant Information Sheet such as rights of correction, length of data storage and destruction procedures and clarify the reason why PLWD and carers are only able to leave the study up to 6 months from signing the consent forms.
2. Information for carers – Please make clear to the carers that any questions they answer will be from their perspective.
3. Page 4 of the carer Participant information sheet – please be clear on the procedure in terms of mailing or calling participants.
4. As confirmed, all participants can consent to decision making. Hence   we suggest that the separate PIS for families is not to seek information from the family members/ carers about the participants, rather it is PIS to inform families.
5. The Researcher noted that participants with mild to moderate dementia are offered the choice to have a family present during the consenting interview, if the participant wishes.
6. Please ensure it is clear in the consent form for participants that someone else is also going to provide information on them via answering the same questionnaires.
7. The consent forms should only include ‘yes’ and ‘no’ tick boxes for matters which are truly optional.
8. The Committee noted that the carer consent form incudes a section which says “I consent to the research staff collecting and processing the information of the person I care for including information about their health” The carer cannot consent to that. Please remove this section.

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* *paragraph 6.22*).
* Please respond to the outstanding ethical concerns detailed above.

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

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| **5** | **Ethics ref:** | **18/NTA/53** |
|  | Title: | Narrow versus standard diameter dental implants |
|  | Principal Investigator: | Dr Momen Atieh |
|  | Sponsor: | International Team for Implantology |
|  | Clock Start Date: | 05 April 2018 |

Dr Momen Atieh was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The aim of this clinical trial is to assess the effectiveness of a narrow diameter dental implant for replacing a single missing back tooth. The narrow diameter dental implant will be compared to standard diameter dental implant in different aspects particularly the need for additional bone graft when placing dental implants.
2. It is anticipated to include 34 participants aged 18 years or older with a single missing back tooth. Several parameters will be recorded throughout the study to explore the advantages and limitations of using either implant size.

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 if both dental implants are used as standard of care in New Zealand. The Researcher confirmed that they are currently being used on patients in New Zealand and have been on the market for 15 years.
2. The Committee queried whether there would be a chance that someone who needs a narrow diameter dental gets a wide diameter dental implant. The Researcher clarified that both types of treatment are considered standard treatment of care and no one would be disadvantaged. Both groups would be susceptible to the same level of risk.
3. The Committee queried why the study is being funded by an International Team for Implantology in Basel, Switzerland and being carried out in New Zealand.
4. The Committee queried whether there are any restrictions on the publications. The Researcher confirmed that there are not any restrictions.
5. The Committee queried who designed the study / research question. The Researcher confirmed that he did.
6. The Committee queried who supplies the dental implants. The Researcher confirmed that the grant money would cover this.
7. The Committee agreed that the study was not sponsored and the ACC statement should be included in the Participant Information Sheet (see below).
8. The Committee asked for clarification on the recruitment and consenting process. The Researcher clarified that an internal referral system from the Urgent Care Unit would refer potential participants to the Researcher who will then assess eligibility. Participants would be given a Participant Information Sheet and consent format the clinic.
9. The Committee noted that the b.1.2. of the application form states that “A titanium and zirconium (TiZr) alloy was recently introduced for fabricating narrow and standard diameter implant to improve mechanical characteristics”. The Committee queried if this combination of metals is currently used. The Researcher confirmed that it is.

Summary of ethical issues (outstanding)

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

1. Please ensure that the study ID is used on the questionnaires and no identifiers.
2. The Committee queried *the* cost of $500 to the participant. The Researcher noted that this cost had been introduced to cover any future maintenance that the participant may need. The Committee asked the Researcher to think about the issue of inducement and coercion when including cost information in the Participant Information Sheet *and whether a cost will exclude some participants.* Studies must have a fair distribution of burden and benefits.
3. Detail on data management in the protocol is lacking. Please provide more comprehensive information as to how study data will managed. Investigators are required to ensure the adequate physical and electronic security of data (*Ethical Guidelines for Observational Studies* paragraph 8.3).

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

1. The Committee suggested using the standard HDEC Participant information sheet and consent form template [https://ethics.health.govt.New Zealand/guides-templates-forms-0/participant-information-sheet-templates](https://ethics.health.govt.nz/guides-templates-forms-0/participant-information-sheet-templates) . This will ensure essential information is included such as the rights of the participants, contact details other than the Researcher, right to access information, etc.
2. Participant Information Sheet – the section “about this study”. The Committee suggested using information in the application form provided in question a.1.5.
3. The Committee noted that page 2 of the Participant Information Sheet refers to standard of care use of bovine bone replacement graft if clinically indicated and highlighted that this would be an issue for vegetarian / vegan participants, those with allergies and religious beliefs. The Researcher confirmed that for vegetarian / vegan participants a synthetic alternative would be used. The Committee would like more information around the use of bovine and the options for alternatives to be included in the Participant Information Sheet. Please ensure this is described in lay language.
4. Please ensure lay language is used in the inclusion/ exclusion criteria of the Participant Information Sheet.
5. Please ensure the “confidentiality “section states that records will be stored for 10 years, not indefinitely.
6. The Committee noted that the consent form states “Personal identifying information will be stored in a secure database at the School of Dentistry at the conclusion of the project for an indefinite period longer than 10-years”. Please ensure data is de-identified and stored against a study code. Please amend the consent form.
7. The Committee noted that the consent form states “I understand that reasonable precautions have been taken to protect data transmitted by email but that the security of the information cannot be guaranteed.” Please remove this from the consent form. It is not acceptable to transfer identifiable data by email.
8. Ethnicity question - The Committee noted that the ethnicity question asked in the demographics questionnaire is incorrect. Please use the Health and Disability Ethnicity Data Protocols standard ethnicity collection question the when collecting ethnicity data to ensure the options available are suitable for New Zealand participants. These classifications are: New Zealand European, Māori, Samoan, Cook Islands Maori, Tongan, Niuean, Chinese, Indian, Other (such as Dutch, Japanese, Tokelauan), Please state: The Committee noted that this question should not be on the consent form. Please move to a more appropriate place, such as the study data collection tool.
9. An ACC statement should be included in the Participant Information Sheet. The Committee suggested the following statement: *“If you were injured in this study, which is unlikely, you would be eligible* ***to apply*** *for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery. If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.”*

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *paragraph 6.22*).
* Please respond to the outstanding ethical concerns detailed above.

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

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| **6** | **Ethics ref:** | **18/NTA/57** **(CLOSED MEETING)** |
|  | Title: | A study comparing the blood levels of two forms of ketamine in healthy volunteers under fasting conditions |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Douglas Pharmaceuticals America Ltd |
|  | Clock Start Date: | 05 April 2018 |

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| **7** | **Ethics ref:** | **18/NTA/59** |
|  | Title: | A Study of the Efficacy and Safety of Guselkumab in Participants with Moderately to Severely Active Crohn's Disease Study to evaluate the safety and effectiveness of guselkumab in people with moderate |
|  | Principal Investigator: | Dr Michael Schultz |
|  | Sponsor: | Janssen-Cilag (New Zealand) Limited |
|  | Clock Start Date: | 05 April 2018 |

Michelle Sullivan 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. This is a large umbrella project, encompassing a Phase 2 and two Phase 2 and 3 trials i.e. GALAXI 1 (Phase 2 study) and GALAXI 2 & 3 (identical Phase 3 studies) and a long term extension.
2. Their primary purpose is to evaluate the safety and efficacy of guselkumab in treating Crohn’s Disease.
3. Another purpose of GALAXI 1 is to find the dose of guselkumab that would be best to use in future studies. Other purposes of GALAXI 2 & 3 are to find the dose of guselkumab that best treats Crohn's Disease and to compare the effects of guselkumab to those of ustekinumab and placebo.
4. It is anticipated that up to 500 participants will be enrolled into GALAXI 1 (ie, 250 in the Initial Dose Decision Cohort and up to 250 in the Transition Cohort) prior to the dose decision. If a dose decision for Phase 3 is not made by the time the 500th patient is randomised, enrolment will be paused until a decision for Phase 3 dosing, or a decision to terminate the development program, is made. Approximately 15 participants in New Zealand.
5. Phase 2((GALAXI 1) ) Intervention groups as follows:
   * Initial Dose Cohort of 250, split into 5 groups
     + Group 1: *Guselkumab Regimen 1 -* 1200mg
     + Group 2: *Guselkumab Regimen 2 -* 600 mg
     + Group 3: *Guselkumab Regimen 3 -* 200mg
     + Group 4: *Active Control, Ustekinumab*
     + Group 5: *Placebo or Ustekinumab Crossover*
   * Transition Cohort of 250
6. Throughout the 3 studies, efficacy, pharmacokinetics, biomarkers, and safety will be assessed at time points.

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 their general concern about umbrella protocols, particularly in this project where the phases overlap significantly.
2. The Committee queried the purpose of the study. Please include more detail in the study Participant Information Sheet to explain what a Phase 2 trial is, the risks it involves and the lack of knowledge about this drug at this dose range in treating Crohn’s disease.
3. The Committee noted that the Data Monitoring Committee will carry out an interim analysis on the Initial Dose Cohort at week 12. Please provide clarification if the results from this analysis inform the start of the Transition Cohort. The Committee would like to see the results of the interim analysis on the Initial Dose Cohort in an interim progress report*.*
4. The Committee will require a progress report at the end of the Transition Cohort before the New Zealand arm proceeds to GALAXI 2 and 3. Please submit this as an amendment, which will require ethics approval before proceeding. This will provide reassurance to participants on safety aspects of the study.
5. The Committee was not willing to approve a long term extension study in this umbrella, this should be a separate application based on good safety information.
6. Safety concerns – the Committee expressed concern over dosing levels as these are much higher than for psoriatic arthritis outlined in the IB. What evidence is there that the higher risk profile as outlined is relevant to the highest dosages? While the Committee is away that monoclonal antibodies as a class have a favourable safety profile, the comparator in this study has serious side effects and the Committee wishes to be assured that participants receive clear safety information.
7. The Committee noted the overlap between phase 2 and 3 and queried if GALAXI 2 and 3 were different, as this information could not be easily found in the PIS or Protocol. Please provide clarity to the Committee.
8. The Committee requested more information on where and how the study samples are being analysed / stored /destroyed. Please provide further details in the protocol.
9. Please provide further details to the Committee as to how new information that may impact a decision to participate will be communicated to participants.
10. Page 15 of main Participant Information Sheet says “No genetic research will be done on your samples “. Please confirm that this is correct for the main study, including mandatory tissue biopsies.
11. Please ensure the protocol includes a section on management of disclosure of significant mental health information that are in the questionnaires.
12. Please review the study questionnaires to avoid repetitive sections.

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

1. There is no mention in the Participant Information Sheet that participants will be split into two cohorts. Please address this.
2. Participants are not informed of the dosages levels nor of the fact that the highest dosage is higher than used in psoriasis studies. Please ensure that participants are fully informed of the dosage levels and the risks*.*
3. Please ensure that participants are fully informed that dosing is monitored.
4. The Participant Information Sheet mentions the known risks. The Participant Information Sheet should be upfront that these risks are known to exist only at dosages lower than what is proposed for this study and in treating a different condition.
5. The Committee noted that while Guselkumab is approved in the USA, EU and Canada for psoriasis and other conditions, it has not been tested on humans with Crohn’s disease. Please ensure this is explicit in the Participant Information Sheet.
6. Main Participant Information Sheet – Please add to the Participant Information Sheet that if a participant is diagnosed with TB or HIV it is a notifiable disease.
7. There is optional sub study at Week 4 which involves an additional procedure - Video ileocolonoscopy with biopsies. This is included in the main Participant Information Sheet and main consent form, however the Committee would like a separate Participant Information Sheet and consent form for this.
8. Please ensure there is a Participant Information Sheet for pregnant participants. Please refer to the Templates section on the HDEC website for suggested wording: <https://ethics.health.govt.nz/guides-templates-forms-0>
9. Please ensure the main Participant Information Sheet uses the suggested HDEC template wording for contraception use (<https://ethics.health.govt.nz/guides-templates-forms-0>). The Committee noted that the child, once born, needs to be reconsented/or consented. The mother cannot consent for the child until it is born.
10. Please ensure the main Participant Information Sheet provides clearer information on compensation cover for study participants.
11. Page 17 of the main Participant Information Sheet – If scientific research on samples is optional please ensure it is clear in the Participant Information Sheet.
12. Page 13 of the main Participant Information Sheet – Under the section “side effects from tests” please remove the wording “are not considered dangerous”
13. Page 13 of the main Participant Information Sheet – Under the section “side effects from tests” please quantify risk of perforation.
14. Page 24 of main Participant Information Sheet – Under the section “Can I get a copy of my medical records?” please remove the sentence relating to participants having to wait until the study is completed. Under the Health Information Privacy Code in New Zealand participants have the right to access and correct information. If this may mean that they are removed from the study this should be stated.
15. Genetic research Participant Information Sheet/Consent form – Please provide information on where the samples are being stored. The leftover blood and the additional blood FUR PIS could be combined into one, they are similar issues, and this would be less confusing for participants.
16. Please ensure there is a section on the consent form to address being sent overseas.
17. Please ensure the different Participant Information Sheets are standalone and include relevant information only for *each* The Future Unspecified Research Participant Information Sheet should only include information relevant to Future Unspecified Research.
18. Use of placebo. It is unclear from the Participant Information Sheet whether those classed as being in the placebo group will stop or continue with their current standard care

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Please provide details on the study design to address the Committee concerns on minimising harm, maximising benefit and meeting other ethical standards (*Ethical Guidelines for Intervention Studies* *para 5.4*).
* Provide details of the Data Safety Monitoring plans *(Ethical Guidelines for Intervention Studies para 6.50).*
* Please respond to the outstanding ethical concerns detailed above in a cover letter

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| **8** | **Ethics ref:** | **18/NTA/58** |
|  | Title: | Proof of Concept Study For Next Generation Intraocular Lens Model MER002 |
|  | Principal Investigator: | MD Dean Corbett |
|  | Sponsor: | Johnson & Johnson (New Zealand) Limited |
|  | Clock Start Date: | 05 April 2018 |

No one from the Research team were 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. Prospective, multi-center, randomized, pair-eye, proof of concept clinical study to evaluate the rotational stability of the test lens IOL, MER002, compared to the control lens IOL, MER000.

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 would like clarification on whether both lenses being used in the study are test lenses.
2. The Committee noted that this is a first in human study but the Researcher had not identified this is an ethical issue in the application form.
3. Please provide clarification on how many sites will be involved in the study. There is conflicting information in the application and the Participant Information Sheet.
4. Data safety monitoring - The application form refers to section 15 of the protocol however there is only reference to a medical monitor and no mention of a data safety monitoring Committee. Please provide more detail around safety monitoring, especially as this is a first in human study. Provide details of the Data Safety Monitoring plans (Ethical Guidelines for Intervention Studies paragraph 6.50).
5. The Committee would like clarification that the study will not be stopped for commercial reasons. Studies should not be terminated simply for reasons of commercial interest or public relations (*Ethical Guidelines for Intervention Studies* paragraph 6.65).
6. The application states that photographs taken in the study are additional and just for use in this study. The Committee would like clarification on whether these photographs will be available for the standard of care treatment of the patient if required.
7. Please advise the Committee which Clinical Trial websites the study will be advertised on.
8. The Committee would like the Researcher to clarify whether they regard it an inducement if the lenses are free compared to what the participant would pay if they went private.

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

1. Please ensure the correct Sponsor is used.
2. Please review the Participant Information Sheet - the Committee noted that information had been cut and paste from another Participant Information Sheet.
3. Please ensure the Participant Information Sheet is pertinent to New Zealand.
4. Please use lay language in the Participant Information Sheet.
5. The Committee would like clarification on how randomisation of the lenses will work. Please ensure this process is clearly explained in the Participant Information Sheet.
6. The Participant Information Sheet mentions video recordings but there is no reference to this in the protocol. Please remove from the Participant Information Sheet.
7. Please move the section on photographing into the section “What does my participation involve”.
8. Page 7 of the Participant Information Sheet – The Committee noted that the amounts are in $US. The Committee suggested removing this table from the Participant Information Sheet and making it clear to the participant that they will get reimbursed for travel costs, etc.
9. Please review / rephrase the statement on page 7 of the Participant Information Sheet “The investigator, Dr. Corbett, has agreed to supervise or personally conduct all testing of the device where human subjects are involved”.
10. Please review and revise the information in the section” what happens after the study or if I change my mind” because it is currently framed in a legalistic manner. Please include a sub-heading on privacy and confidentiality. Legalise information need to be reviewed, particular the disclosure of authorised service providers and third parties. Please remove the reference to “data collected and entered into the Case Report Forms” as this is not standard information provided to participants. Please move the statement “No biological specimens will be collected during the research study” to a more appropriate section of the Participant Information Sheet.
11. Please remove Americanism, such as IRB, from the Participant Information Sheet.
12. Please include clearer information on what happens to the participant if they withdraw from the study.

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* *paragraph 6.22*).
* Please provide more detail around data safety monitoring.
* Please respond to the outstanding ethical concerns detailed above.

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

## General business

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

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| **Meeting date:** | 15 May 2018 |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

1. **Problem with Last Minutes**

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

The meeting closed at 5.20pm