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|  | Minutes |

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| **Committee:** | | Northern A Health and Disability Ethics Committee | | | | | | |
| **Meeting date:** | | 09 June 2015 | | | | | | |
| **Meeting venue:** | | Novotel Ellerslie | | | | | | |
| **Time** | **Item of business** | | | | | | | |
| 1.00pm | Welcome | | | | | | | |
| 1.05pm | Confirmation of minutes of meeting of 12 May 2015 | | | | | | | |
| 1.30pm | New applications (see over for details) | | | | | | | |
|  | i 15/NTA/65  ii 15/NTA/66  iii 15/NTA/67  iv 15/NTA/68  v 15/NTA/70  vi 15/NTA/72  vii 15/NTA/73  viii 15/NTA/75 | | | | | | | |
|  |  | | | | | | | |
| 5.00pm | General business:  Noting section of agenda | | | | | | | |
| 5.15pm | Meeting ends | | | | | | | |
| **Member Name** | | | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |  |
| Dr Brian Fergus | | | Lay (consumer/community perspectives) | 01/07/2012 | 01/07/2015 | Present |  |
| Ms Susan Buckland | | | Lay (consumer/community perspectives) | 01/07/2012 | 01/07/2015 | Present |  |
| Ms Shamim Chagani | | | Non-lay (health/disability service provision) | 01/07/2012 | 01/07/2015 | Present |  |
| Mr Kerry Hiini | | | Lay (consumer/community perspectives) | 01/07/2012 | 01/07/2015 | Present |  |
| Ms Michele Stanton | | | Lay (the law) | 01/07/2012 | 01/07/2015 | Present |  |
| Dr Karen Bartholomew | | | Non-lay (intervention studies) | 01/07/2013 | 01/07/2016 | Present |  |
| Dr Christine Crooks | | | Non-lay (intervention studies) | 01/07/2013 | 01/07/2015 | Present |  |
| Mr Mark Smith | | | Non-lay (intervention studies) | 01/09/2014 | 01/09/2015 | Present |

## Welcome

The Chair opened the meeting at 1.00pm and welcomed Committee members.

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 May 2015 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **15/NTA/65** |  |
|  | Title: | Antibiotics in acute diverticulitis |  |
|  | Principal Investigator: | Associate Professor Ian Bissett |  |
|  | Sponsor: | University of Auckland |  |
|  | Clock Start Date: | 28 May 2015 |  |

Rebekah Jaung and Prof Ian Bissett in person 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

* The study investigates whether antibiotics are required for low risk (uncomplicated) cases of diverticulitis. It will compare antibiotics (standard therapy) verses placebo.
* Prior studies that compared antibiotics with no treatment indicated that there was no difference.
* The researchers explained that they are enrolling patients after conducting the gold standard scan to determine the level of diverticulitis.
* The study will exclude anyone who is allergic to the antibiotics being used, anyone who has a compromised immune system, anyone who has inflammatory bowel disease, anyone who has complicated forms of diverticulitis, and anyone with a high pain score (>6/10).

The researchers explained the group being studied has a low risk of complications overall. The researchers have conducted a retrospective observational study that identified a number of additional factors that are associated with worse outcomes for this patient population, this informed the exclusion criteria. This protects against any undue risk for participants.

Summary of ethical issues (resolved)

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

* The researchers explained that they have equipoise and justified their use of a placebo.
* The researchers explained that prior studies support the hypothesis for this study.
* The Committee asked if participants had to stay in hospital for any additional time. The researchers explained that participants go home as usual. At Auckland hospital it usually takes about 3-4 days after which participants will be able to go home - this is determined by the Auckland City Hospital doctors. The researchers confirmed a participant was not required to be an inpatient for 7 days to participate, and in fact the primary end point in length of stay in hospital (powered to detect one day’s difference).
* The researchers confirmed the study team meets on a fortnightly basis to monitor safety information and study progression, but that patients will be seen by the site investigators twice a day initially and then once a day till discharge.
* The researchers explained that in current practice everyone on admission receives a standard set of blood tests. The doctor may request further blood tests depending on how the patients are doing. There should not be any additional blood tests for study participation.
* The researchers stated if there were complications for participants occurring after enrolment their inclusion in the trial would be reconsidered.
* Please explain the use of data for future research. Researchers explained that data will be kept for 10 years then destroyed. If they wanted to extend this research it would be useful to use data generated from this study, however this data would be stripped of identifiers.
* Please explain the risk of developing complicated diverticulitis, particularly if antibiotics are not administered. The researchers explained their hypothesis, that antibiotics are not necessary, is informed by prior trials. There was no evidence to support the view that a lack of antibiotics was associated with development of disease.
* The researchers clarified that the information that is held during study, after the unblinding and up to the 30 day follow up will be key-linked information that can be linked back to identifiable information. After the study the data will have identifiers removed.
* The Committee asked about the placebo manufacturer. The Researchers explained their ongoing work with pharmacy to create practical placebos for oral, also intravenous delivery given the need to maintain blinding. They have gone back to the manufacturers to develop an appropriate formula.
* The Committee asked about Maori prevalence for the disease. The researcher explained that they have New Zealand population data on acute levels. Rates among Maori were proportional to non-Maori.
* The difficulty with this particular patient population and ethnicity is that the disease is primarily age related.
* The Researchers confirmed that the researcher will not be the patient’s treating clinician.
* The Committee asked how long the participants have to consider participation. The researchers stated they wished to enroll patients within 24 hours, noting it was an acute situation. At Auckland hospital patients have CT scan within 16 hours for diverticulitis. There is an 8 hour gap between that scan and enrolment.
* The researchers acknowledged the acute setting and stressed they would approach participants and try and give them as much time as possible. The researchers explained that it was difficult to conduct an RCT in an acute setting. Getting treatment started as soon as possible as well as giving enough time to consider participation is difficult but they believe they have found an appropriate balance.
* The researcher confirmed that treatment will not be withheld during the period of time where patients consider participation. If empiric antibiotics are given by the admitting doctors the patient would not be eligible for the trial. Because antibiotics are delivered at different times from admission across the three hospitals, and empiric antibiotic use is still possible, the researchers have worked at each site to develop protocols so low risk patients are not given antibiotics initially. If antibiotics are required early they will have them early - treatment will not be held up for the study – although these patients are likely to be more unwell or in pain (suggesting complicated disease) and therefore unlikely to be eligible. The Committee suggested clarifying the protocol to reflect this.
* Please explain the concurrent observational study - is this a separate set of patients? The researchers explained that the consent process for that study is separate but it may well involve same patients. The investigator will clearly identify the different studies, their voluntary nature, and the different risks for the intervention trial.

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

* Please make it clear in the PIS that the study will go towards the PhD qualification of a co-investigator.
* The Committee noted the primary outcome is length of stay, whereas the PIS covers a lot about whether antibiotics are necessary. Please consider informing participant about what the study aims are - the participants should know about the reduced hospital stay measure. Please also make it clear participants don’t need to stay in hospital any longer than standard practice.
* Include some more information about randomisation.
* The Committee confirmed that the data would only be used to inform future research. The Committee noted that the PIS/CF implies that the researchers are asking for permission to use identifiable data to conduct unspecified future research. Please make it clear that this will be de-identified data.

Decision

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

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| **2** | **Ethics ref:** | **15/NTA/66** |  |
|  | Title: | Effect of warm humidified carbon dioxide on bacteria in a surgical wound |  |
|  | Principal Investigator: | Mrs Jessica Fogarin |  |
|  | Sponsor: | Fisher & Paykel Healthcare |  |
|  | Clock Start Date: | 28 May 2015 |  |

Mrs Jessica Fogarin was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of ethical issues (resolved)

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

* The Committee queried how the DSMC will work noting the CI is the data monitor. Mrs Fogarin explained that this conflict was raised prior to the HDEC meeting and had subsequently been changed. Monitoring arrangements will be passed from CI to the other colleagues. This measure mitigates the conflict bias.
* The Committee asked if this (warm humidified carbon dioxide) was standard treatment. Mrs Fogarin explained it was not standard of care at Auckland Hospital. It is available commercially for purchase and is used internationally. It is also used at Waikato Hospital. It is just not used in Auckland.
* What is the reason for the study? Mrs Fogarin explained the study investigates the impact of this system specifically on bacterial load. The current benefit is due to reducing heat loss - that is the benefit of using this system however it remains unclear whether the application of CO2 impacts the number of bacteria in the wound.
* The Committee requested justification of blinding patients. Mrs Fogarin explained there are a number of observations that are taken the day post healing - they don’t want the participants to be biased about how they treat or describe their own wound.
* Please explain how safety is monitored, who will install the device? The CI will set up and install the device. The surgeon and anesthetist will be involved in terms of putting the device in the participant. Mrs Fogarin confirmed that the surgeon, Mr John Windsor, is an investigator.
* Will the surgeon be the same for all participants? Mrs Fogarin stated yes, only 10 participants.
* What are the criteria for stopping the study, particularly with respect to safety? Mrs Fogarin stated there are no known side effects or safety issues. The system is standard practice at many other sites and widely used internationally. It will be at the discretion of the surgeon to stop the use of this device for any clinical reason.
* The researcher confirmed that the indemnity process occurs during the locality process. It is part of the RRC process.
* The researcher confirmed that this study will go through the ADHB Maori review group.
* Please clarify what swabs were being taken. The researcher explained that swabs would be taken the following day. The Committee was satisfied with the explanation.

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 feels that the responsibility for the patients should lie with Dr Windsor, as Dr Windsor will have the sole responsibility for conducting the trial in theatre and the care of the participants the principal investigator responsibilities would sit better with him. Prescreening and identification of potential patients should be the responsibility of the institution not the sponsor.
* The sponsor should not have access to medical records.
* The recruiting responsibilities should be with a research nurse and Dr Windsor to further protect patient confidentiality.
* The Committee noted that insurance is expired. The researcher explained it had been renewed and it would be uploaded.
* The Committee asked how participants are identified and how does the consent process occur. Mrs Fogarin stated initially it was a research nurse who was approaching participants. However it was changed to be CI who is recruiting during potential participant’s elective upper GI procedure meetings. Mrs Fogarin stated they would review medical records to identify who might be eligible. Mrs Fogarin explained the hospital agreed to release this information for the purposes of screening and recruiting for the study. Only data relevant to inclusion and exclusion criteria will be released. Please detail what data will be released.
* The Committee noted that usually an independent party will talk with potential participants and if interested they are referred to the CI. The Committee stated they are not comfortable with the CI meeting with the potential participant. The researcher agreed they would amend their screening and recruitment process to have an independent research nurse or clinician make the first contact.
* Please provide the Committee with further details on the:

Trials oversight

Safety oversight

Patient identification

Patient screening

Consent process - How will conflict /coercion be mitigated if treating doctor is recruiting doctor

Trial procedures

* Patient confidentiality

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

* Please add information on compensation if something does go wrong.
* Please add will not cost ‘you’ on page 4 of PIS.
* Please add surgeon details if he is an investigator, as well as a research nurse contact details.
* Please remove jargon.
* Please explain in the PIS that the CI or a research nurse will be present in procedure to fill out case report form.
* Please explain the ASA score for participants.
* Please amend the dates in the PIS/CF that are currently incorrect.
* Please amend title of organisation to Medicines New Zealand, pg.4.
* Add where the laboratory is for participants.
* Please amend ‘made anonymous’ to de-identified.
* Please remove the last section of ACC that relates to non-commercial trials.
* Pg.5 - storage of study records. Who will be responsible for storing study related material? The researcher explained the company has secure storage facilities - fire proof, confidential etc. The researcher confirmed it would be de-identified data, no medical records. Just completed case reports. There are systems to ensure continuity. Committee suggested adding information about the document control center that looks after data.

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).
* Explain how the conflict of interest resulting from care provider being the researcher is addressed *(Ethical Guidelines for Intervention Studies para 4.19)*
* Address outstanding ethical issues in a cover letter

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

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| **3** | **Ethics ref:** | **15/NTA/67** |  |
|  | Title: | The GEM Project |  |
|  | Principal Investigator: | A/Prof Dr Michael Schultz |  |
|  | Sponsor: | University of Toronto |  |
|  | Clock Start Date: | 25 June 2015 |  |

A/Prof Dr Michael Schultz 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

* The study investigates Crohn’s disease. In New Zealand there are 15,000 people who have an inflammatory bowel disease. About half have Crohn’s disease. There is a genetic component but environment plays a role.
* It is not generally known why people get Crohn’s disease.
* Patients who have a first relative who has Crohn’s disease have a higher chance of getting it themselves.
* This project will find patients with Crohn’s disease and ask them if they have first degree relative who may be interested in participating - primarily children, brothers or sisters.
* The study will assess genetics, environmental questionnaires - everything that is need for a baseline. The healthy relatives will then be followed for initially 6 years with phone calls. If they have a diagnosis of Crohn’s disease or have any symptoms the researcher will run through whole raft of measurements again and will re-assess the relative to try and find out how they differ from the patients who do not get Crohn’s disease.
* The majority of first point relatives will not get Crohn’s disease.
* This study started several years ago in Canada. Drop outs and movements have made recruitment difficult. It is also running in Israel, the UK and Australia is starting the ethics process.

Summary of ethical issues (resolved)

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

* The Committee queried how 500 New Zealand participants will be recruited. Dr Schultz stated 500 is very optimistic. The Crohn’s foundation is supportive and has been very active in getting patients to get together online. The plan is initially to recruit patients here in Dunedin - they have about 50 potential participants who may be eligible. They would then engage the Crohn’s foundation in Wellington.
* Where is data being sent? Dr Schultz confirmed all data is sent to Canada. It is entered into a database in Dunedin where it is de-identified prior to being sent to Canada. Blood and urine samples will be pretreated in Dunedin and then sent to Canada for storage.
* Dr Schultz confirmed that the tissue is destroyed after 25 years adding the tissue is not used for any other research.
* Dr Schultz confirmed that the budget for New Zealand was set by the Canadian group. Funding is also set by the Canadian research group.
* Please clarify - is this blanket consent or broad consent, for research for Crohn’s disease related studies. Dr Schultz explained it was broad, however the Committee noted that it was worded ‘any’ research. This must be changed so it restricts the research within the bounds of Crohn’s or inflammatory bowels disease. The researcher agreed.

Summary of ethical issues (outstanding)

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

* Dr Schultz explained there is a 3 month grace period for the potential for relatives to change their minds. The committee queried if data is deleted, citing the protocol pg.8 which states it will be kept but ‘locked’ in the database. Dr Schultz understanding was that it was only 3 months and then deleted but would check with the sponsor.
* Please add ethnicity data collection. Ensure collection questions (Environmental Risk Assessment) are appropriate for a New Zealand setting/context - please refer to the New Zealand census ethnicity and ancestry questions.
* The Committee noted that it was unclear about what is different between proband and the other participants. It must be very clear in the introduction of each PIS to explain why the person is being approached and what will be required of them.
* Please submit any advertising for the study including the Facebook advertising.

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

* The Committee noted that the PIS is currently worded as an assent form. There should be a PIS for parents consenting for their children, and child assent form that is age appropriate.
* Add that all samples are stored in Canada - none in New Zealand. Make this explicit across all PIS.
* Please amend proband to a lay language term.
* The Committee noted that in New Zealand 16 year olds can consent.
* Please add standard ACC clauses relating to New Zealand.
* Please keep data for children for 10 years after they turn 16.
* The Committee stated it should be clear that if participants don’t want to provide samples then they can’t participate.
* 25 years in PIS verses 15 years in the consent form. Please clarify storage length.
* Please remove the word subjects. Refer to participants.
* Be consistent about disposal measures for tissue.
* The PIS text is mixed between the Crohn’s suffer and the relative - please review as they are currently confusing.
* Please add some information on the tissue storage facilities.
* The Committee noted in the risks section for bio banking relates to informational and privacy risks, and cultural risks. Please add more information.
* The Committee noted that the PIS are currently fairly Canadian / American. Please amend and review for referral to legislation that is irrelevant to a New Zealand context.
* The Committee noted that further information on tissue being sent overseas is required. Please ensure the following requirements are included:

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| **Future Unspecified Research (FUR) and Bio banking - note these are requirements for FUR** |
| * an indication of the type and nature of the research to be carried out and its implications for the donor, where possible, and an explanation of why the potential donor is being approached for their tissue and specifically what tissue is being sought. |
| * known possible researchers or institutions that might use the tissue sample, if possible. |
| * whether the donor’s sample is going to be, or is likely to be sent overseas, and where possible, to what country or countries. |
| * acknowledgement that all future unspecified research in New Zealand will be subject to ethical review. However, when a tissue sample is sent overseas, unless it is sent in conjunction with a New Zealand research project, future research is likely to be considered by an overseas ethics committee without New Zealand representation. |
| * whether the donor’s identity and details will remain linked with the sample or whether the sample will be de-linked. |
| * a statement that if a donor consents to a tissue sample being unidentified or de-linked, they relinquish their right to withdraw consent in the future. |
| * whether the donor may be contacted in the future regarding their tissue sample. Whether or not, and under what circumstances, information about the future unspecified research will be made available to the donor and/or (where relevant) their clinician. |
| * acknowledgement that the donor will not own any intellectual * property that may arise from any future research. |
| * whether there is provision to withdraw consent for the use of human tissue samples in the future. Where there is provision to withdraw consent, only tissue samples remaining at the time of a request to withdraw and any information held for future unspecified research may practically be withdrawn. Tissue samples or information used in research before the request to withdraw is received is unlikely to be able to be returned or * destroyed. |
| * acknowledgement that the donor’s decision regarding the consent for use of their tissue sample for unspecified future research will in no way affect the quality of a donor’s current or future clinical care. |
| * where and for how long a tissue sample will be stored, how it will be disposed of and whether there is a cultural protocol for its disposal. For example, information about the institution holding the tissue sample: its aims, research procedures and research governance. |
| * whether or not tissue samples could be provided to other researchers and institutions, and whether or not such provision could include sending samples to other countries |
| * whether or not collected samples will be provided to commercial biomedical companies or will be used in commercial research collaborations, if known. |
| * what provisions will be made to ensure patient confidentiality. |
| * that different cultural views may inform choice about donation of tissue; for example, for some Maori, human tissue contains genetic material that is considered to be collectively owned by whanau, hapu and iwi. |
| * that cultural concerns may arise when tissue samples are sent overseas, including how tissue samples are stored and disposed of. Processes for monitoring and tracking what happens to samples may not be acceptable to donors. |
| * that donors may want to discuss the issue of donation with those close to them, for example; family, whanau, hapu and iwi. |

Decision

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

* Please submit copies of any advertisements. If they are not prepared please submit when they are ready, as amendments
* 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*).
* Address outstanding ethical issues in a cover letter

This following information will be reviewed, and a final decision made on the application, by Dr Mark Smith and Mr Kerry Hiini.

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| **4** | **Ethics ref:** | **15/NTA/68** |  |
|  | Title: | Validation of Test of Masticating and Swallowing Solids (TOMASS) |  |
|  | Principal Investigator: | Ms Wan Tian Ng |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 28 May 2015 |  |

Ms Wan Tian Ng 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

* The study measures the ability to swallow solids for patients who have had a stroke and experience swallowing difficulty.
* The TOMASS test was created by the CI supervisor and her colleagues. The aim is to provide an alternative for further exploration- non-invasive, less expensive and easily administered test cf to current videoscopy.
* Although the application is proposed as an intervention study it is an observational study.

Summary of ethical issues (resolved)

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

* Ms Ng explained prior studies that looked at what happened when healthy participants had anesthetic injected into their mouth and tried to chew and swallow.
* Ms Ng confirmed she was a clinician-speech therapist (SLT) but her role in this study is as a masters student. (Note –Speech Therapists are not registered under the Health Practitioners Competence Assurance Act).
* Ms Ng confirmed that only participants who need an x-ray already are recruited.
* The Committee requested information on recruitment. Ms Ng explained that clinicians will be briefed on what kind of patients to look for. When a patient comes in for the videoscopy the clinical process will remain unchanged. After the x-ray we will know whether they are eligible - they will be asked if they would like to participate. Once this is over the researcher (CI) will come and do the informed consent process. Patients will have due time to consider participation in the study and do not have to agree on the spot, they can return at a later time.
* How will the videos be used? Ms Ng explained that there is a program that is used to measure the swallowing. This gives objective measurements. Videos will be kept for 10 years in a secure storage environment. After which they will be destroyed.
* Ms Ng confirmed that in the TOMASS test video the patient is not identifiable (the video only captures lower part of jaw).
* Please explain your understanding of the peer review comments. Ms Ng explained that they will amend the study to meet the suggestions. The Committee asked about the inclusion and exclusion criteria suggestions. Ms Ng explained that they had talked with their supervisor about this, explaining that the videoscopy will act as a means of screening that should be sufficient.

Summary of ethical issues (outstanding)

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

* Please explain consent processes for vulnerable populations, and the intention to recruit patients who cannot consent for themselves via family consent. Ms Ng explained that the aphasia PIS is for those who have difficulty reading as a result of their stroke. Ms Ng stated they will gauge understanding by talking to potential participants.
* The Committee noted that it could not approve observational research of this nature on unconsented participants. After discussion Ms Ng confirmed that they will only include participants that can provide individual consent and understand study related information (either PIS). The Committee requested some information on how they will judge whether participants can consent or not.
* Ms Ng explained that the clinician will likely assist in the determination of whether a potential participant would be able to consent or not. The Committee felt this was appropriate and requested this in writing.

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

* Please reword that this is masters level research.
* Please amend that it is a quarter of a biscuit.
* On page 21 - it is not clear whether Maori research review will occur. The researcher explained that a letter of approval has been received. No changes were requested.
* The Committee requested that ethnicity information is collected from participants.
* Please add ACC clause for the PIS.
* Make it clear that withdrawal clause for participation is only valid until procedure occurs.
* Please make clear they can only withdraw data up until a point as this is a master’s project and any information will be included in that (recommend specifying a date of withdrawal to ensure the masters research can be completed).
* Add a clause on the consent form requesting to use data that has already been gathered - namely the videoscopy.
* Add information on destruction of data by her supervisor.
* The Committee noted that consent should include time to decide to participate or not. The researcher noted the participants do have time to consider, and don’t need to do it straight away. The Committee requested that information is included in the PIS.

Decision

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

* Please amend the information sheet and consent form, and assent forms, taking into account the suggestions made by the Committee (Ethical Guidelines for Observation Studies para 6.11).
* Provide process to recruit potentially vulnerable persons in writing.
* Address outstanding ethical issues in a cover letter

This following information will be reviewed, and a final decision made on the application, by Dr Mark Smith and Ms Susan Buckland.

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| **5** | **Ethics ref:** | **15/NTA/70** |  |
|  | Title: | SHIELD Trial |  |
|  | Principal Investigator: | Dr Andrew Holden |  |
|  | Sponsor: | Symic Vascular, Inc |  |
|  | Clock Start Date: | 27 May 2015 |  |

Dr Andrew Hill, Dr Andrew Holden via teleconference. and Ms Donna Katae 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

* Study is classed as a First in Man device, where as it is more less standard angioplasty device but delivering a drug.
* Peripheral Artery Disease (PAD) is a common circulation problem in which the arteries that carry blood to the legs becomes narrowed. The most common cause of PAD is atherosclerosis.
* Atherosclerosis is often referred to as a hardening of the arteries and can be caused by a buildup of fatty deposits in the walls of the leg arteries which in term restrict blood flow.
* With angioplasty a balloon is inserted into the blocked artery and inflated – pushing the fatty deposits outward against the artery wall.
* There will be 2:1 randomisation to the treatment arm.
* SBCV is comprised of modified heparin and will be excreted via the kidneys with preclinical studies showing SBCV was no longer present at the site of angioplasty 28 days post treatment.
* Pilot trial to look at safety, which the researchers don’t think will be a significant issue, and early efficacy study between the two groups.

Summary of ethical issues (resolved)

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

* The angioplasty device is a standard device, and the drug is known drug with known side effects. The drug will be directed at an artery site, but in doing so will enter the general stream. That is why it is important the drug is safe in its own right.
* Confirmed that SCOTT has been sought.
* The researchers confirmed the drug is flushed (not injected).
* Is there any chance the ‘stickiness’ of the modified drug is going to cause a problem? The researchers confirmed there is no risk. The only risk is bleeding and this will be accounted for in the lower leg.
* The researcher confirmed the dose for efficacy is similar to regular standard use and same dose as standard practice. The Committee suggested that this could be useful information for patients, preferably on pg.2.
* The Committee noted the 30 days statement could be confusing for participants.
* The Committee suggested doing some formatting changes and thinking about the headings used for clarity re the procedures for the two groups.
* The Committee confirmed additional angiogram is additional to standard of care. Make this clear.
* The Committee thanked the researchers for their peer review.
* Please explain how DSMC will work. Researchers explained DSMC is not yet established but will be established closer to the time of it starting. There will be one. An independent medical monitor will also be involved in reviewing the data. The researchers stated it is likely that there are plans in place which they can report back to the Committee.
* The researchers confirmed a CRO will be involved.
* Please explain who is reviewing the whole study process and who is on the trial management committee? The researcher explained that the monitoring of primary end points etc. will be established. Researcher explained that they would send further information to HDEC.

Decision

This application was *approved* by consensus.

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| **6** | **Ethics ref:** | **15/NTA/72** |  |
|  | Title: | BR.31 |  |
|  | Principal Investigator: | Dr David Gibbs |  |
|  | Sponsor: | Christchurch Hospital |  |
|  | Clock Start Date: | 28 May 2015 |  |

Dr David Gibbs 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. The Committee decided that she would stay in the room but that Dr Karen Bartholomew would present and take the role of lead reviewer.

Summary of Study

* Therapeutic intervention study after lung cancer treated by surgery.
* RCT to receive either an immunotherapy drug or placebo.
* Aim of study to see whether experimental treatment improves outcomes in patients.
* Phase III. 1000 patients around the world. Four in New Zealand.

Summary of ethical issues (resolved)

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

* Dr Gibbs confirmed there were additional CT scans.
* Please explain ‘followed until the end of your life’. Dr Gibbs explained that secondary outcomes will be mortality. Long term follow up will occur for this study. The participants will not be coming in for follow up - it concerns mortality data. The Committee accepted this justification.
* Dr Gibbs explained side effects of this class of drug appear to be mild to moderate, clinically. People may experience severe side effects, the most common of which is inflammation of the gut. Locally they have not had any serious episodes of that, these have been reported internationally.
* Are you satisfied with the DSMC arrangements? Dr Gibbs confirmed the researchers were.
* Dr Gibbs confirmed the study is investigator led. Funding goes through to Sydney. Commercial involvement is supply of drug but study is not sponsored.
* The Committee asked if the peer review resulted in any changes to protocol. Dr Gibbs responded there was not.
* The Committee commended the PIS, in particular that it identified divergences from standard of care.
* The Committee noted that lung cancer disproportionately impacts Maori. The responses to the application questions relating to Maori did not adequately reflect this point. It is of vital importance to have Maori in the study, and the issue of tissue collection is important for Maori and needs to be given more thought and consultation.
* The Committee asked about the necessity for the whole tissue block to be sent overseas. The ethical concern is that if patients fail this trial, they may be eligible for other trials and tissue will be needed for this. Sending the whole block may prevent participants being involved in other research. If this is the case please note the significance in the PIS.
* The Committee asked if researchers had considered that tissue could be reviewed locally. Dr Gibbs explained that overseas analysis is mandatory - this is where they analysis the protein.
* Is the FUR for additional or leftover samples (of blood)? Dr Gibbs stated an additional sample. This needs to be noted in the PIS.
* Please explain the data that support this trial. Dr Gibbs explained that there is evidence in advanced disease that you see large numbers of lung cancer patients responding to these drugs. For instance about 30% of patients received measurable tumor shrinkage. This lead to sustained shrinkage for these patients. Everyone is trying to get these drugs into phase III setting and early disease setting.
* Are you satisfied with the data to start these trials given that the 500 patients on the drug worldwide are still in phase II with no interim efficacy data yet available? Dr Gibbs explained that he was due to experience with this class of drug, but noted there is a question mark around the long term safety which will only come clear after 10 years. The drugs work by switching on the immune system. This runs the possibility of longer term mortality or disease. There is no indication that this is the case, however this is why we are conducting long term follow up for these patients.
* Dr Gibbs explained that our current treatment for lung cancer is not great with a high recurrence rate and death.

Summary of ethical issues (outstanding)

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

* Please explain the SCOTT waiver. Researcher was unsure about the justification of this, waivers had been accepted by SCOTT in the past. Please clarify with relation to communications to SCOTT.
* The Committee noted that it is possible for Maori not to participate if those conditions are required. Dr Gibbs explained that the tissue block is not necessarily the whole specimen - it is some representative part thereof. It is more that the overseas laboratories like to process from start to finish for good practice measures.
* Dr Gibbs stated there is no mention of return of tissue in the protocol. The Committee requested that this requirement is clarified with the research group, noting this is also a barrier for Maori.
* Please explain the statement about collecting information even if a participant withdraws, does this relate to the mortality data and outcomes? The Committee requested clarification on this in the PIS.
* The Committee noted that the cultural issues section of the application is inadequate. Please re-answer these questions in a cover letter.

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

* ACC information requires updating.
* Section 11 - ‘rest of your life follow up’ - like AIWH. This is Australian - please revise for international information and jargon.
* Please explain randomisation for patients.
* Please amend privacy legislation (or any reference to legislation generally), ensuring it reflects a New Zealand context.
* Please add that mortality data will be accessed.

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| **Future Unspecified Research (FUR) and Biobanking - note these are requirements for FUR** |
| * an indication of the type and nature of the research to be carried out and its implications for the donor, where possible, and an explanation of why the potential donor is being approached for their tissue and specifically what tissue is being sought. |
| * known possible researchers or institutions that might use the tissue sample, if possible. |
| * whether the donor’s sample is going to be, or is likely to be sent overseas, and where possible, to what country or countries. |
| * acknowledgement that all future unspecified research in New Zealand will be subject to ethical review. However, when a tissue sample is sent overseas, unless it is sent in conjunction with a New Zealand research project, future research is likely to be considered by an overseas ethics committee without New Zealand representation. |
| * whether the donor’s identity and details will remain linked with the sample or whether the sample will be de-linked. |
| * a statement that if a donor consents to a tissue sample being unidentified or de-linked, they relinquish their right to withdraw consent in the future. |
| * whether the donor may be contacted in the future regarding their tissue sample. Whether or not, and under what circumstances, information about the future unspecified research will be made available to the donor and/or (where relevant) their clinician. |
| * acknowledgement that the donor will not own any intellectual * property that may arise from any future research. |
| * whether there is provision to withdraw consent for the use of human tissue samples in the future. Where there is provision to withdraw consent, only tissue samples remaining at the time of a request to withdraw and any information held for future unspecified research may practically be withdrawn. Tissue samples or information used in research before the request to withdraw is received is unlikely to be able to be returned or * destroyed. |
| * acknowledgement that the donor’s decision regarding the consent for use of their tissue sample for unspecified future research will in no way affect the quality of a donor’s current or future clinical care. |
| * where and for how long a tissue sample will be stored, how it will be disposed of and whether there is a cultural protocol for its disposal. For example, information about the institution holding the tissue sample: its aims, research procedures and research governance. |
| * whether or not tissue samples could be provided to other researchers and institutions, and whether or not such provision could include sending samples to other countries |
| * whether or not collected samples will be provided to commercial biomedical companies or will be used in commercial research collaborations, if known. |
| * what provisions will be made to ensure patient confidentiality. |
| * that different cultural views may inform choice about donation of tissue; for example, for some Maori, human tissue contains genetic material that is considered to be collectively owned by whanau, hapu and iwi. |
| * that cultural concerns may arise when tissue samples are sent overseas, including how tissue samples are stored and disposed of. Processes for monitoring and tracking what happens to samples may not be acceptable to donors. |
| * that donors may want to discuss the issue of donation with those close to them, for example; family, whanau, hapu and iwi. |

Decision

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

* Updated separate Participant Information Sheet and Consent Form for the use of tissue for future unspecified research (*Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes, para 2*).
* 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*).
* Clarify whether tissue can be returned from overseas and whether some tissue can be kept for clinical purposes.
* Address outstanding ethical issues in a cover letter

This following information will be reviewed, and a final decision made on the application, by Dr Mark Smith and Ms Susan Buckland and Brian.

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| **7** | **Ethics ref:** | **15/NTA/73** |  |
|  | Title: | ReLeaf Feasibility Study |  |
|  | Principal Investigator: | Dr Andrew Holden |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 28 May 2015 |  |

Dr Andrew Hill, Dr Andrew Holden and Ms Donna Katae 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

* The Researchers explained the different trial designs for the medical devices. For the ReLeaf study the device is not an alternative to an existing procedure, as there is really no other treatment options for people with this condition.
* The technical process for the procedure was explained.
* Valve technology is only used for legs.
* This is a multicentre, feasibility and safety study to treat patients who have deep vein problems as a result of chronic venous insufficiency (CVI).
* First in Human device.

Summary of ethical issues (resolved)

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

* The Committee queried if this technique had been used in animals? The researchers explained that it is difficult to test any venous interventions on animals. There is too much difference in anatomy. The researchers will clarify the animal testing that has occurred, if any. The Researchers confirmed device demonstrations have occurred in cadaveric specimens, and that this is a much better model.
* Inability to have anticoagulation is an exclusion criteria. There is some additional risk due to the instrument positioning.
* A radiation assessment has been requested. The Committee was satisfied with this.
* The Committee commended the PIS, adding the pictures were very helpful.
* The Committee noted on page 5 there is some medical jargon. Please explain in lay language.
* Thank you for the peer review. Please explain whether the comments from peer review were incorporated into the study. The Researchers confirmed that the comments had been taken into account. There was one question that the researchers would respond to HDEC about. Please include in a covering letter.
* What is the greatest risk with this study? The researchers explained increased pressure could occur in the calf and foot. The vein could be injured, resulting in blockage or obstruction. This would make symptoms worse. There may be some treatment options in this scenario. The second important risk was of Deep Vein Thrombosis leading to pulmonary emboli (rarely resulting in death). Thrombotic risk was noted with the open surgical procedure, and remains a risk with this procedure. The mitigation is the anticoagulant process in the protocol. The researchers stated that any deep vein procedures carry a risk of thrombosis.
* The researchers explained that currently for this disease there is no alternative treatment.
* The testing for the concept has primarily occurred in cadaveric studies.
* How will you train for this procedure? The researchers explained the bench top models they use to practice and prepare. While there is plenty of practice and preparation but there are always unforeseen risks.
* Will there be any video or live streaming of the procedure? The researchers stated cameras will record the procedure.
* The researchers discussed options to treat participants if anything went wrong with the study.
* Researchers stated that based on their experience the benefits outweigh the risks.
* The Committee asked if researchers will have any trouble recruiting? The researchers explained that the patients are seen in clinic and they are aware of a small number of participants who could benefit. They are only looking for a small sample size. Any larger projects would require more screening. No issue to be perceived with this size.
* The plan is to recruit two, determine that the procedure is technically feasible, no safety issues are identified, and is beneficial and following this recruit a further 10.
* The Committee asked why there were 2 participants. The researchers explained that this mitigated the risk of losing their one participant as there are possibilities to abandon the procedure during surgery if they are deemed unsafe to participate due to quality of veins.
* Committee requested an official update after 2 participants prior to moving to the further 10 participants.

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

* The surgical procedure risks are well documented. Please explain the anticoagulation risks and radiation risks.
* Revise ACC information.
* Change to Medicines New Zealand regarding compensation statement.

Decision

This application was *approved* by consensus.

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| **8** | **Ethics ref:** | **15/NTA/75 (CLOSED)** |  |
|  | Title: | A study to investigate pembrolizumab in patients with metastatic triple-negative breast cancer (mTNBC). |  |
|  | Principal Investigator: | Dr David Porter |  |
|  | Sponsor: | Pharmaceutical Company |  |
|  | Clock Start Date: | 28 May 2015 |  |

Dr David Porter 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 conflict of interest. The Committee decided that Dr Crooks could remain in the room for discussion of this application.

Summary of Study

* The study investigates a novel antibody that is artificially manufactured. The antibody binds to a protein (which is important as it is the signal that stops the body from reacting against the cancer in an immune response).
* Roughly 20% have responded to treatment in a small study. The expression of this protein has some correlation with effectiveness of treatment.
* One study question is to determine if these drug treatments are futile for some groups of patients.

Summary of ethical issues (resolved)

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

* The Committee discussed other sites internationally with the researcher.
* Dr Porter confirmed that a SCOTT application has been submitted.
* The Committee queried about the size of the dose, asking whether it was quite large for every 3 weeks. The researcher explained that this dose had been in other studies and shown to be safe, and higher doses in some other studies. The researchers had no particular concerns.
* With the sampling - could you please include specific information on where the samples are being sent. pg.7
* Are there any risks of rebound for these drugs? Dr Porter explained that there is no data to support that view yet.

Summary of ethical issues (outstanding)

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

* Please explain DSMC plans in place. Please clarify the monitoring arrangements in place to ensure safety for participants.
* Dr Porter explained that cancer trials often require blood and genetic material. The tests that are set out to be done from the beginning are well thought out and comprehensive. The future biomedical research is an issue where if they consent but then withdraw their blocks will be destroyed. They are working with sponsor to try and only send some slides of the block and keep some for clinical purposes. The issues with tissue blocks being sent overseas, and not being available if patients want to participate in other future trials, were noted. The Committee felt this was appropriate and requested a response from the sponsor.
* Please explain what happens when withdrawal occurs? Dr Porter explained that samples will be destroyed. We are talking to the sponsor about returning samples. The Committee felt this was appropriate and requested this was followed up.
* The Committee queried how long tissue should be stored for the mandatory biomarker testing. Please clarify.
* Please update insurance information, currently expired. Submit to HDEC with your response.

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

* As a general comment, the PIS is written as a legal document and is not particularly inviting for a participant to read. We accept the need for pregnancy statements, but surely they don’t need a whole page and can be written in a more succinct manner?
* The Committee would support any effort by the researcher to make the PIS more participant friendly. Please inform the Sponsor of our concern. The second page of exclusion criteria in particular seems an unusual and non-invitational practice that the Committee does not support. The Committee will be looking closely at the clarity and understandability of such PIS’s (to the participant) in any future applications, and sponsors should take these concerns on board.
* Please be clear what kind of data is being sought for long term survival data. Include this information in the PIS.
* Please revise the storage of data from 50 years to a more appropriate duration eg 15-20 years.
* Please make it clear that CT scans are additional to standard care.
* Photographs on page 13 - ‘how will my privacy be protected’. Are these tumor pictures? Dr Porter stated they were not aware of any photographs that would identify a person. Perhaps measuring skin legions. Please clarify this for participants, where it is placed it (between age etc) seems like an identity photo.
* Research medicines have changed their name to Medicines New Zealand. Please amend.
* Please add summary about the cohorts, rather than referring to ‘cohort B’.
* Add investigator details.
* Include a separate, optional PIS for biobanking with the requirements below:

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| **Future Unspecified Research (FUR) and Biobanking - note these are requirements for FUR** |
| * an indication of the type and nature of the research to be carried out and its implications for the donor, where possible, and an explanation of why the potential donor is being approached for their tissue and specifically what tissue is being sought. |
| * known possible researchers or institutions that might use the tissue sample, if possible. |
| * whether the donor’s sample is going to be, or is likely to be sent overseas, and where possible, to what country or countries. |
| * acknowledgement that all future unspecified research in New Zealand will be subject to ethical review. However, when a tissue sample is sent overseas, unless it is sent in conjunction with a New Zealand research project, future research is likely to be considered by an overseas ethics committee without New Zealand representation. |
| * whether the donor’s identity and details will remain linked with the sample or whether the sample will be de-linked. |
| * a statement that if a donor consents to a tissue sample being unidentified or de-linked, they relinquish their right to withdraw consent in the future. |
| * whether the donor may be contacted in the future regarding their tissue sample. Whether or not, and under what circumstances, information about the future unspecified research will be made available to the donor and/or (where relevant) their clinician. |
| * acknowledgement that the donor will not own any intellectual * property that may arise from any future research. |
| * whether there is provision to withdraw consent for the use of human tissue samples in the future. Where there is provision to withdraw consent, only tissue samples remaining at the time of a request to withdraw and any information held for future unspecified research may practically be withdrawn. Tissue samples or information used in research before the request to withdraw is received is unlikely to be able to be returned or * destroyed. |
| * acknowledgement that the donor’s decision regarding the consent for use of their tissue sample for unspecified future research will in no way affect the quality of a donor’s current or future clinical care. |
| * where and for how long a tissue sample will be stored, how it will be disposed of and whether there is a cultural protocol for its disposal. For example, information about the institution holding the tissue sample: its aims, research procedures and research governance. |
| * whether or not tissue samples could be provided to other researchers and institutions, and whether or not such provision could include sending samples to other countries |
| * whether or not collected samples will be provided to commercial biomedical companies or will be used in commercial research collaborations, if known. |
| * what provisions will be made to ensure patient confidentiality. |
| * that different cultural views may inform choice about donation of tissue; for example, for some Maori, human tissue contains genetic material that is considered to be collectively owned by whanau, hapu and iwi. |
| * that cultural concerns may arise when tissue samples are sent overseas, including how tissue samples are stored and disposed of. Processes for monitoring and tracking what happens to samples may not be acceptable to donors. |
| * that donors may want to discuss the issue of donation with those close to them, for example; family, whanau, hapu and iwi. |

Decision

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

* Please provide a separate Participant Information Sheet and Consent Form for the use of tissue for future unspecified research (*Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes, para 2*).
* 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 details of the data safety monitoring plan *(Ethical Guidelines for Intervention Studies para 6.50).*
* Please submit evidence of sponsor insurance. *(Ethical Guidelines for Intervention Studies para 8.4).*
* Address outstanding ethical issues in a cover letter

This following information will be reviewed, and a final decision made on the application, by Dr Shamim Chagani and Ms Michelle Stanton.

## General business

1. The Committee noted the content of the “noting section” of the agenda.

* The Committee discussed the Ethics in Practice conference, the Maori Health Research and Biobanking Conference and talked about the book ‘The Politicisation of Ethical Review in New Zealand’.
* The Committee discussed the article provided by an HDEC member on the rationale of design for studies involving medical devices.
* The HDEC secretariat updated the Committee on appointments for Ministry staff.

1. The Chair reminded the Committee of the date and time of its next scheduled meeting, namely:

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| **Meeting date:** | 14 July 2015, 08:00 AM |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

The following members tendered apologies for this meeting.

* Dr Mark Smith
* Ms Michele Stanton

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 4.45pm