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| **Committee:** | Southern Health and Disability Ethics Committee |
| **Meeting date:** | 15 March 2016 |
| **Meeting venue:** | Sudima Hotel, Christchurch Airport, 550 Memorial Drive, Christchurch |

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| **Time** | **Item of business** |
| 12:00pm | Welcome |
| 12:05pm | Confirmation of minutes of meeting of 16 February 2016 |
| 12:30pm | New applications |
|  | i 16/STH/22  ii 16/STH/24  iii 16/STH/25  iv 16/STH/26  v 16/STH/27 |
| 2:20pm | General business:   * Noting section |
| 2:30pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Ms Raewyn Idoine | Lay (consumer/community perspectives) | 27/10/2015 | 27/10/2018 | Present |
| Mrs Angelika Frank-Alexander | Lay (consumer/community perspectives) | 27/10/2015 | 27/10/2018 | Present |
| Dr Sarah Gunningham | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | Present |
| Dr Nicola Swain | Non-lay (observational studies) | 27/10/2015 | 27/10/2018 | Present |
| Dr Mathew Zacharias | Non-lay (health/disability service provision) | 27/10/2015 | 27/10/2018 | Present |
| Dr Devonie Eglinton | Non-lay (intervention studies) | 01/07/2013 | 01/07/2016 | Present |
| Assc Prof Mira Harrison-Woolrych | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | Present |
| Dr Fiona McCrimmon | Lay (the law) | 27/10/2015 | 27/10/2018 | Present |

## Welcome

The Chair opened the meeting at 12:00pm 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 16 February 2016 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **16/STH/22** |
|  | Title: | Sleep in Kids with Diabetes: the SKIDDoo Study |
|  | Principal Investigator: | Associate Professor Esko Wiltshire |
|  | Sponsor: |  |
|  | Clock Start Date: | 03 March 2016 |

Associate Professor Esko Wiltshire was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This study investigates the interaction between sleep and Type 1 diabetes in young people.
2. The goal of this study is to help develop methods of detecting potential problems before they progress to more serious complications.
3. This study involves 75 participants aged 5-18 with diabetes, matched to a control participant without diabetes. The total study size is 150 participants across the two arms.

Summary of ethical issues (resolved)

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

1. The Committee appreciated the further information that was provided regarding peer review following an email from the Secretariat.
2. The Committee questioned whether the researchers are aware of a similar study being conducted in Auckland. The Researcher confirmed that they are aware of this study and may collaborate where possible.
3. The Committee noted that this study includes participants aged between 5 and 18 years old and the consent forms indicate that parental consent is intended to be obtained for all participants. However, he Committee stated that although participants may be physically adolescents for the purpose of the study, some participants are legally adults and must consent to their own participation in the study, rather than having their parents’ consent on their behalf. Specifically, all participants aged 16 years and over must consent to their own participation in the study, and some participants who are under 16 may also be mature enough to provide their own informed consent. The Researcher agreed to adjust the consent requirements accordingly.
4. The Committee questioned whether it was appropriate for participants’ parents to complete the questionnaire regarding their adolescent’s sleep if the adolescent was consenting to be in the study for themselves. The Researcher agreed that they would either provide a questionnaire for the participant to fill in about their own sleep or explain clearly in the Participant Information Sheet that the participant’s parent will be asked to complete this questionnaire to ensure that the participant is fully informed regarding what is involved in the study.

Summary of ethical issues (outstanding)

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

1. The Committee requested that a very simple assent form for young children is produced with pictures to help explain the study.
2. Please reword the Participant Information Sheets for Children as they do not need to contain information about ACC or reimbursement for transport. The Committee noted that although some of these sections may be included in the template, that they are not always necessary for child assent forms as these forms need to only include information that will help the child understand what they are agreeing to do.
3. The Committee suggested the addition of a photograph of the equipment required to be worn may be beneficial as the participants may not know what this is.
4. The Committee noted that currently all participants are being asked to provide assent and have their parents consent to their participation. The Committee stated that participants aged 16 years and older must consent for themselves and should have their consent considered as legally equivalent to that of an adult. Further, some participants under 16 years old may be competent to provide their own informed consent. Please develop a suitable information sheet and consent form for participants who are able to consent for themselves.
5. Please add information to the Participant Information Sheets regarding the questionnaire that will be completed about the participant’s sleep. Please ensure this includes information for the adolescent participants who are consenting for themselves regarding what is involved with their sleep questionnaire and who will be completing this.
6. Please adjust the ethnicity question in the questionnaire to ensure it is suitable for New Zealand participants. The Committee suggested the New Zealand Census question on ethnicity may be an appropriate one to use.
7. Please ensure that all health information is stored for a minimum period of 10 years after each participant turns 16 (Health (Retention of Health Information) Regulations 1996). The Committee noted that as it is common for all of the study data to be discarded at the same time that this may mean that the study data is kept for 10 years after the youngest participant turns 16. Please ensure that it is clear in the Participant Information Sheets for parents and older children how long the study data will be stored.
8. Please proof read the information sheets to ensure accuracy. The Committee noted that at times the form for control participants refers to ‘your child’ and this is not appropriate as this is the form for the child rather than the parent. Also, at times, the parents’ Participant Information Sheet refers to ‘you’ rather than ‘your child’.
9. In the information sheets for older participants and parents please include how many participants are being recruited.
10. Please remove the yes/no tick boxes from the consent forms for any points that are not truly optional. These tick boxes should only apply to statements where the participant could select ‘no’ and still participate in the study.
11. The Committee noted that some statements (taken from the HDEC template) in the information sheets and consent forms are pointers directed at researchers and should be removed. Please carefully consider these forms to ensure these statements are removed as they are not intended for participants.
12. The Committee noted that the parent form asks whether the participant may have a friend that can also participate in the study, they suggested that if siblings are able to participate that this should be mentioned in this form too.
13. Please add page numbers and footers to the information sheets and consent forms.
14. Instead of referring to mother/father in the parent forms this should refer to the participant’s parent or caregiver to ensure it is appropriately inclusive.
15. If study results or data may be shared with other researchers, such as the similar study in Auckland, please ensure that this is stated in the information sheets where appropriate, such as a forms for older children and parents.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the committee (Ethical Guidelines for Observational Studies para 6.10).

This following information will be reviewed, and a final decision made on the application, by Dr Sarah Gunningham and Mrs Angelika Frank-Alexander.

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| **2** | **Ethics ref:** | **16/STH/24** |
|  | Title: | Comparison of the blood levels of two forms of bexarotene capsule in healthy male volunteers under fed conditions |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Douglas Pharmaceuticals America Ltd |
|  | Clock Start Date: | 03 March 2016 |

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

Potential conflicts of interest

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

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

Summary of Study

1. This study involves comparing the bioavailability of bexarotene tablets from two manufacturers.
2. Study participants will take a tablet from one manufacturer on one weekend and then the following weekend they will take a tablet from the other manufacturer.
3. Participants will need to stay at the study site overnight from Friday evening to Saturday morning each weekend.
4. The Committee stated that they are impressed by the improved quality of the applications from these researchers.
5. The Committee commended the investigators for providing participants with condoms for the duration of the study and for one month after the last dose.
6. The Committee commended the excellent peer review included with this study and noted that it was thorough and well thought out.

Summary of ethical issues (resolved)

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

1. The Committee questioned why participants must be male. The Researcher explained that the study drug is known to cause birth defects and they do not want to run this risk with female participants.
2. The Committee questioned the rate of reimbursement for this study as although participants only need to stay at the study site overnight on study weekends the study restrictions apply for the whole study period. The Researcher stated that they believe the $1400 reimbursement is reasonable given the study requirements and is based on their calculations of a rate of $15 per hour and participants will be sleeping for most of the time they are required to be at the study site.

Summary of ethical issues (outstanding)

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

1. The Committee noted that due to the specific risk of birth defects, the need for participants to inform their sexual partners and wear condoms should be more prominent in the Participant Information Sheet and Consent Form. Please put the statements about contraception higher up in the risks and benefits section. Please reword the language in the consent form to ensure it is clear that participants need to inform **any** sexual partners that they are involved in this trial. Please also add to the study inclusion criteria and the study restrictions section of the PIS that participants need to use condoms for the duration of the study and for one month after the last dose of bexarotene.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the committee *(Ethical Guidelines for Intervention Studies para 6.22)*.

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| **3** | **Ethics ref:** | **16/STH/25** |
|  | Title: | Zenflow Study |
|  | Principal Investigator: | Professor Peter Gilling |
|  | Sponsor: | Zenflow, Inc. |
|  | Clock Start Date: | 03 March 2016 |

Ms Rana Reuther was present by teleconference for discussion of this application. She gave apologies for Professor Peter Gilling who was unable to attend the teleconference.

Potential conflicts of interest

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

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

Summary of Study

1. This study is a first in human trial of the Zenflow device for men with benign prostatic hyperplasia (BPH) who have failed medical treatment.
2. The use of this device is proposed as an alternative to surgery and the researchers claim it may fix BPH during a five minute flexible cystoscopy procedure. It is hoped that this device can provide a permanent solution.
3. Initially this device will be inserted in theatre and then once they are more familiar with the procedure they intend to insert it under local anaesthetic as an outpatient surgery procedure.

Summary of ethical issues (resolved)

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

1. The Committee noted that the application states that the device imbeds in the urethral wall but that it does not cause any tissue damage. They questioned how the device imbedded in the urethral wall without tissue damage. The Researcher explained that it does not go into the tissue but the shape of the device allows the urethral wall to form around it because it puts pressure on the wall and pushes into it, but it does not pierce the tissue.

Summary of ethical issues (outstanding)

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

1. The Committee questioned the testing that had previously been done in animals and human cadavers. The Researcher explained that she was unsure of the exact details and the Co-ordinating Investigator would be able to answer these questions, however, unfortunately he was unable to attend the meeting. The Committee noted that they required more information from Professor Gilling before they could proceed with the approval of this study.
2. The Committee noted that previous similar devices had problems with tissue growing around the device and making it difficult to remove without damage. The Researcher explained that the device is made out of material that helps to prevent the growth of tissue around the device.
3. The Committee questioned how long the device had been left in animals in previous tests. The Researcher was unable to provide this information.
4. The Committee noted that the application stated that it was hoped that this device would be an advance on previous stents that had a number of issues and asked what these issues are and how this device avoids them. The Researcher explained that the main issue with previous stents has been tissue growth around the device making removal difficult. The Committee noted that although these devices are meant to be permanent solutions, there may be complications that lead to the need to remove. Please provide further detail regarding these and the expected frequency of such complications.
5. The Committee noted that infection is a possible reason for removal being required, they questioned the rates of infection that were expected with this device.
6. The Committee noted the possibility of nerve damage and associated incontinence and requested more information on these complications, including if the device needs to be removed.
7. The Committee questioned whether ongoing follow up beyond one year was intended as the Participant Information Sheet states that follow up visits will be at 3, 6, and 12 months. The Committee noted that annual follow up seemed essential and requested confirmation that this would be the case.
8. The Committee questioned who would cover costs related to the ongoing follow up and possible removal of the device, if this was needed in the future.
9. The Committee noted that all three peer reviewers of this application are not independent of the study investigators and sponsor. Please provide further evidence of appropriately independent external peer review.
10. The Committee questioned if this trial would have staggered roll-out of the device, for example will one participant receive this device some time before any others to allow the researchers to observe any unexpected complications following insertion before it is inserted in a number of participants.
11. Please provide more information regarding the previous testing of this device in animals and cadavers.
12. Please provide more information on the problems encountered with previous devices prior to removal (for example efficacy rates and frequency of complications such as bleeding, infection, nerve damage etc). Please also explain why they do not expect to encounter these same problems with this device.
13. The Committee questioned what practical training will be available for urologists implanting this device in the study. The Researcher stated that a representative from Zenflow will attend the first few insertions. The Committee questioned who this representative would be and what urological surgical experience they may have. The Committee questioned whether the representative would have had experience inserting the device in a cadaver or animal and knowledge of the expected differences to inserting the device in live human tissue.
14. The Committee questioned why this study is being first conducted in New Zealand and Bulgaria only.

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

1. Please include more information on possible complications in the Participant Information Sheet, such as infection, nerve damage, and incontinence. This information should be informed both by previous studies with this device and with other similar devices. Alternatively, if it is truly not possible to give any information on the expected rates of complications please state this in the information sheet.
2. The Participant Information Sheet does not clearly state that this is a first in human study. Please ensure this is made clear at the beginning of the form.
3. The Committee noted that it is important to explain that the device will first be implanted in some participants in theatre and then into other participants as an outpatient procedure as some participants may only wish to become involved once the device has been implanted in some other people first. Please state in the Participant Information Sheet how many people will have it implanted in theatre and how many participants will have it implanted as an outpatient procedure.
4. Please make it clearer in the Participant Information Sheet that this is a permanent device which will remain in place for many years. .
5. The Committee suggests including a picture showing the actual size of the device in the information sheet.
6. Side effects and/or risks need to be closer to the top of the Participant Information Sheet risk section. These must include specific statements, for example describing the risk of complications such as bleeding, infection, migration, nerve damage, incontinence, and how often they may be expected to occur. This information can be based on other stents if necessary, but should state the risks quoted are as experienced with other stents and the risks with the new device may be higher or lower.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the committee (Ethical Guidelines for Intervention Studies para 6.22).
* Please provide evidence of independent peer review of the study protocol (Ethical Guidelines for Intervention Studies Appendix 1).
* Please respond to the Committee’s outstanding ethical concerns detailed above. The Committee suggests that it may be appropriate to respond to these concerns in a detailed cover letter to the Committee.

This following information will be reviewed, and a final decision made on the application, by the full Southern Health and Disability Ethics Committee.

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| **4** | **Ethics ref:** | **16/STH/26** |
|  | Title: | PADDI |
|  | Principal Investigator: | Dr Martin Misur |
|  | Sponsor: |  |
|  | Clock Start Date: | 03 March 2016 |

Dr Martin Misur and Ms Davina McAllister were present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This study involves randomly assigning participants to the study drug, dexamethasone, a drug used for treating nausea and vomiting after operation, but the participant’s anaesthetists may alter their care based on clinical judgement.
2. The Committee commended the high quality of the Participant Information Sheet and Application. The Committee stated that the application form had been completed thoughtfully with good answers to all questions including the questions regarding Maori consultation and possible cultural issues.
3. This study involves 12,000 participants worldwide with approximately 8,800 participants in New Zealand.
4. This study has already received ethics approval overseas.

Summary of ethical issues (resolved)

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

1. The Committee questioned the purpose of this study. The Researcher explained that the aim of the study was to test the safety and side effects of a drug that is already commonly used in Australia and New Zealand.
2. The Committee questioned the recommended dose of the study drug in standard care. The Researcher explained that it ranges between 4 and 8mg, with some anaesthetists using a per kg method to determine dosage and others using between 4 and 8mg on every patient. The Researcher stated that this study involves using 8mg as they have found that this is a common dose recommended in recent studies.

Summary of ethical issues (outstanding)

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

1. The Committee requested that it is clarified in the Participant Information Sheet that standard of care may involve the use of this drug and that standard dosing is between 4 and 8mg and that this study is specifically testing an 8mg dose.
2. Please ensure it is clear in the Participant Information Sheet that this study is not intended to find a benefit from the study drug, rather it is looking to study the safety and rate of side effects, and participants should not expect additional benefit from their participation.
3. The Committee noted that the point in the Consent Form regarding participants’ records being accessed for study auditing is overly complex and needs to be simplified.
4. The Consent Form contains some duplication, please revise to remove this.

Decision

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

* 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*).

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| **5** | **Ethics ref:** | **16/STH/27** |
|  | Title: | Tenecteplase versus Alteplase for Stroke - TASTE |
|  | Principal Investigator: | Dr John Newton FINK |
|  | Sponsor: | The University of Newcastle |
|  | Clock Start Date: | 04 March 2016 |

Dr John Newton Fink 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 study is to test the hypothesis that patients who have experienced an acute hemispheric ischaemic stroke who have a penumbra on perfusion CT or MRI within 4.5 hours of symptom onset will have less disability at 3 months when treated with intravenous Tenecteplase compared to intravenous Alteplase. The Committee stated that they were pleased that the researcher had been able to provide some information to the secretariat prior to the meeting regarding the non-consensual nature of this study and the ability of the study to meet Right 7.4 of the HDC Code of Rights.
2. This study is being done as Alteplase has been used for this purpose since 1995 and clinicians have been looking for a better alternative for a number of years. Tenecteplase is a new thrombolytic treatment already approved to treat heart conditions and this study intends to investigate whether it is useful for treating ischaemic stroke.
3. This study follows a pilot study from Australia that found a benefit from the use of Tenecteplase in this patient group.
4. The Researchers believe that Tenecteplase will have a benefit for patients beyond Alteplase, which is standard of care. However, a full study has not yet been done and is not being sponsored by the manufacturer of Tenecteplase as Alteplase is also produced by the same company. More research is required to satisfy regulatory authorities regarding the efficacy of this drug for this indication.
5. Some participants in this study may be unable to provide informed consent due to suffering a stroke.

Summary of ethical issues (resolved)

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

1. The Committee stated that it is not possible for HDECs to approve an application unless it is consistent with New Zealand law, including the right not to be subjected to medical or scientific experimentation without that person's consent (section 10 of the New Zealand Bill of Rights Act 1990). Research involving participants who are not competent to consent is inconsistent with the Bill of Rights unless it is undertaken in accordance with Right 7 (4) of the of the Code of Health and Disability Services Consumers’ Rights. In addition to requirements regarding ascertaining the views of the consumer and other suitable persons (forms consistent with this aspect are currently included in this application), Right 7(4) of the Code requires that any health services provided without the informed consent of the consumer must be in the best interests of the consumer. This means that there must be some benefit, or potential benefit, to the participant beyond what they would receive if they were not participating in the research.
2. The Committee asked if the researcher could confirm whether this study meets the best interest requirement of Right 7(4) of the HDC code of Rights. The Researcher stated that their clinical judgement is that participants have a potential benefit from being in the study because the chance of benefit from the study drug is introduced by being in the study. If participants are randomised to the control group they will receive standard care, however, the researchers have reason to believe that study arm is better and the only way for these patients to receive this study drug is by being part of this study. The researcher stated that because study involvement means there is a chance of getting better treatment then this fulfils the best interest requirement of Right 7.4 of the HDC Code of Rights.
3. The Committee questioned whether the researchers would do the 3 month follow up with the participant’s friends or family if the participant was unable to complete this aspect of the study. The Researcher stated that this was not suitable for this study and they would only complete this follow up with the participant directly.
4. The Committee questioned the risks of bleeding with this study drug. The Researcher stated that the pilot study found lower rates of bleeding compared to standard care.
5. The Committee questioned whether this use of the study drug is approved anywhere for treatment of ischaemic stroke. The Researcher stated that it is not yet approved to treat stroke victims anywhere.

Summary of ethical issues (outstanding)

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

1. Please remove the note to the researcher regarding stating if an interpreter is available from the Consent Form.
2. Please rename the ‘proxy’ information sheet as this implies that the family or friend completing this form is legally providing consent on the participants behalf, however this is not possible in New Zealand. The Committee suggests calling this the ‘Friends and Family Information Sheet’.

Decision

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

* 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*).

## 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:** | 19 April 2016, 12:00 PM |
| **Meeting venue:** | Dunedin International Airport, Maungatua Room, 25 Miller Road, Momona, Dunedin |

The following members tendered apologies for this meeting.

* Mrs Angelika Frank-Alexander and Dr Sarah Gunningham

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 2:30pm