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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 11 February 2014 |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

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| **Time** | **Item of business** |
| 1.00pm | Welcome |
| 1.10pm | Confirmation of minutes of meeting of 10 December 2013 |
|  | New applications (see over for details) |
| 1.30-1.50pm  1.50-2.10pm  2.10-2.30pm  2.30-2.50pm  2.50-3.10pm  3.10-3.30pm  3.30-3.50pm  3.50-4.10pm | i 14/NTA/12  ii 14/NTA/4  iii 14/NTA/7  iv 14/NTA/10  v 14/NTA/11  vi 14/NTA/13  vii 14/NTA/16  13/NTA/217 |
| 4.10-4.30pm | General business:   * Noting section |
| 4.30pm | Meeting ends |

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| **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 | 01/07/2014 | Present |
| Mr Kerry Hiini | Lay (consumer/community perspectives) | 01/07/2012 | 01/07/2014 | Present |
| Dr Etuate Saafi | Non-lay (intervention studies) | 01/07/2012 | 01/07/2014 | Apologies |
| Ms Michele Stanton | Lay (the law) | 01/07/2012 | 01/07/2014 | 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 |

## Welcome

The Chair opened the meeting at 1.05pm and welcomed Committee members, noting that apologies had been received from Dr Etuate Saafi

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 10 December 2013 were confirmed.

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| **1** | **Ethics ref:** | **14/NTA/4** |
|  | Title: | Endometrial Carcinoma – A Retrospective Study at a Single Community Hospital |
|  | Principal Investigator: | Dr Susan Bigby |
|  | Sponsor: |  |
|  | Clock Start Date: | 30 January 2014 |

Dr Susan Bigby was 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 ethical issues

The main ethical issues considered by the Committee were as follows.

* Dr Bigby explained that she is seeing increasing numbers of women under 50 with endometrial cancers and that this is a result of the impact of oestrogen and obesity on endometrial cancers. She noted that this particularly affects Pacific women (rates of 60 per 100,000 compared with 16 per 100,000 for all New Zealand women) and that this was unique to South Auckland. This study will create a register of approximately 600 women, with the objective of analysing them by five year age groups based on BMI and ethnicity. It is hoped that this will allow her to identify a high risk vulnerable population.
* Dr Bigby explained that currently if a woman goes to a doctor with irregular bleeding, tissue diagnosis is only done she is over the age of 40. She noted that if a profile can be developed of women more likely to get endometrial cancer, then EC could be diagnosed earlier and clinicians could use a different treatment.
* Dr Bigby noted that she is seeking ethical approval for her use of the database and that if clinicians want access to it, they will need to seek ethics approval.
* The Committee asked whether a misdiagnosis could be found when looking at the slides. Dr Bigby confirmed that this possibility could not be excluded.
* The Committee asked whether women should be re-consented. Dr Bigby advised that she will be looking at slides going back to about 1996 and that people may have moved or died. She explained that this was a problem that was unique to South Auckland and could potentially save lives. The Committee agreed that the benefits of the study outweighed the risks of not re-consenting patients.
* The Committee asked how long slides would be kept for under standard care. Dr Bigby advised that they are kept indefinitely in the public system and 20 years in the private system.
* The Committee asked if there was a risk of people being stigmatised. Dr Bigby believed that rather than stigmatising them, this information would be used to help them.
* Dr Bigby confirmed that this study would be heard at the next Māori Research Review Committee.

Decision

This application was *approved* by consensus.

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| **2** | **Ethics ref:** | **14/NTA/7** |
|  | Title: | Reduced-dose rivaroxaban in the long-term prevention of recurrent symptomatic venous thromboembolism (VTE). |
|  | Principal Investigator: | Dr Mark Smith |
|  | Sponsor: | Bayer New Zealand Ltd |
|  | Clock Start Date: | 30 January 2014 |

Dr Mark Smith was present by teleconference for discussion of this application.

Potential conflicts of interest

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

Dr Christine Crooks declared a potential conflict of interest, and the Committee decided that she would not take part in the discussion.

Summary of ethical issues

The main ethical issues considered by the Committee were as follows.

* Dr Smith explained that this study will focus on the secondary prevention of blood clots using rivaroxaban. Participants would have previously had a blood clot and have been given the usual anticoagulant treatment. They would then be given the option of continuing anticoagulation treatment.
* This study will investigate whether aspirin, 10g rivaroxaban or 20g rivaroxaban is the most effective and safest way of preventing blood clots. If the lower dose of rivaroxaban provides good results, this would mean less risk of bleeding for patients.
* The Committee asked what the standard dosage of rivaroxaban is currently. Dr Smith advised that the 20g dose is the recommended treatment for active clots and the 10g dose is recommended for the prevention of clots following orthopaedic surgery.
* The Committee asked if ethical approval was being sought in any other country. Dr Smith advised that it was he was unsure of the status of these applications. He confirmed that he would be happy to start the study when ethical approval is received, rather than waiting for all countries to get approval.
* The Committee asked if it was usual for a doctor to receive payment for referring participants to the study (R.5.5). Dr Smith advised that he was not aware of this and thought it would be unusual for this to happen.
* The Committee asked how participants would be recruited to the study. Dr Smith explained that participants would be referred to through the haemostasis service, which manages patients after the diagnosis of a blood clot. He advised that there is also the ability to email GPs alerting them to clinical trial if they have a patient who fits the inclusion criteria and might be interested.
* Dr Smith confirmed that several DHBs in New Zealand will be used for this study.
* The following changes were requested to the PIS and consent form:
  + Please remove references to “fake matching placebo tablets” on page 3 of the PIS as this is not a placebo trial.
  + Please include wording in the PIS that participants should check with their health insurer that they are covered to participate in the trial.
  + Please include risks to women getting pregnant while in the study in the PIS.

Decision

This application was *approved* by consensus subject to the following non-standard approval conditions being met.

* Please amend the PIS and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies, para 6.22).*

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| **3** | **Ethics ref:** | **14/NTA/10** |
|  | Title: | A Study of RG1662 in Adults and Adolescents with Down syndrome (CLEMATIS) |
|  | Principal Investigator: | Prof Ed Mitchell |
|  | Sponsor: | Roche Products New Zealand Limited |
|  | Clock Start Date: | 30 January 2014 |

Professor Ed Mitchell was 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 ethical issues

The main ethical issues considered by the Committee were as follows.

* The Committee asked for the link between this study and the 13/NTB/35 study and key issues around consenting for participants. Professor Mitchell explained that the 13/NTB/35 study was a screening protocol to see if they could identify participants who might be clinically eligible for entry into a subsequent study. At the screening, patient’s medical history was taken, along with a clinical exam, nurses took blood pressure, height and weight, an ECG and administered two psychological tests. Professor Mitchell advised that the patients had to pass psychological tests as the study will look at improving cognition and if a participant was unable to speak, it is unlikely that the study medication would take a non-verbal person to verbal.
* The screening study involved one visit to see whether people would be eligible for the study. He advised that they now had eight people, with the potential to take two more people for the treatment study.
* The Committee asked for the ages of the potential participants. Professor Mitchell advised that Roche were aiming for half adults and half adolescents. He explained that the younger age group is more difficult to recruit to as parents are more protective.
* The Committee asked if the pre-screening was consented. Professor Mitchell confirmed that it was. He explained that in his opinion, none of the participants, had sufficient cognitive ability to understand the details of the study so parents consented on their behalf and the participants assented.
* The Committee asked what difference improved memory would make to people with Down syndrome. Professor Mitchell explained that it will improve their memory, cognitive function, language skills and could possibly lead to more independent living.
* The Committee asked how participants had been found for the previous study (13/NTB/35). Professor Mitchell explained that one of his research fellows had done another study, which looked at why people with Down syndrome were overweight. A database was created and people within the appropriate age range were contacted. Professor Mitchell advised that participants’ parents had given a general consent to be re-contacted for future research.
* The Committee asked about the Phase 1 research. Professor Mitchell advised that 180 healthy participants and 30 participants with Down syndrome had been given the drug.
* The Committee noted the length of the scheduled study visits (six hours), and that this could be difficult for participants. Professor Mitchell advised that Auckland Clinical Services will employ a play therapist from Starship Hospital for those visits.
* The Committee asked if Professor Mitchell had any safety concerns about the drug. He advised that he will be telling participants that this is a new drug and while preliminary work suggests that it has the usual side effects, as it has only been given in a small number of people, major side effects cannot be excluded.
* The Committee asked why the dosage was calculated by age rather than by weight. Professor Mitchell explained that if it was done by weight it would done by lean body mass and as people up to 18 years are still growing, it would be more appropriate to use a smaller dose.
* The Committee thought it was essential that GPs are aware that their patients are participating in the study. Professor Mitchell explained that in his experience participants always consent to this but he would be happy to make this compulsory.
* The Committee believed that the parent’s questionnaire was quite intrusive and asked for the rationale behind it. Professor Mitchell explained that Down syndrome has a huge impact on families and if this study drug improves a participant’s ability to function, this may reduce stress in the family.
* The Committee were concerned about the suicidality worksheet for a study which looks at memory. Professor Mitchell explained that the study drug works on the same receptor that Benzodiazepine works on and this is known to increase the risk of suicidality. The Committee advised that this information would need to be included in the PIS.
* Professor Mitchell confirmed that SCOTT approval has been applied for.
* The Committee advised that cultural issues for Māori relating to tissue and blood samples need to be included in the PIS. Professor Mitchell explained that while Māori were not excluded, no Māori participants had been identified during screening. The Committee advised that it would be useful during recruitment to look at who might benefit from the study and take this into account when recruiting.
* Professor Mitchell advised that Māori consultation had been undertaken.
* The Committee focused on the issue of adults who are unable to give informed consent, bearing in mind the letter from the Office of the Health and Disability Commissioner which stated that it was “unlikely that Right 7(4) permits the participation of incompetent consumers in clinical trials that are not lifesaving or designed to prevent serious damage to health.”
* The Committee were concerned the participants lack the capacity to consent. For participants over the age of 16, the Committee has concerns that under New Zealand law, no one else can legally consent on their behalf. Welfare guardians under the Protection of Personal and Property Rights Act 1988 are only able to consent on their behalf for potentially lifesaving treatment or treatment that prevents serious damage to health.
* The Committee asked if it was necessary to include biobanking in the study. Professor Mitchell explained that it was to analyse the genetic profile of participants to determine why drugs worked for some, and not others.
* Professor Mitchell explained that he believes that the benefits of this study outweigh the risks as at present there is nothing that treats cognitive performance in people with Down syndrome and this meets the best intervention standard.
* The Committee noted that the study medication is not available beyond the end of the trial and asked, if the drug worked, what would happen to participants when they were taken off the drug. Professor Mitchell advised that he is having discussions with Roche about this.
* The Committee advised that as samples will be from unconsented participants, samples can be used for pharmacokinetic testing but not biobanking. As the biobanking samples will be sent overseas, the Northern A HDEC has no jurisdiction over these.
* There is no current therapeutic option for the treatment of cognitive deficits in individuals with DS. Hence the trial is aimed at assessing any possible improvement in quality of life for DS participants and caregivers. (similar drugs have shown promise with Alzheimers disease).
* The Committee decided that the decision be deferred pending further legal advice on issues relating to consent. Depending on the legal advice received, the Committee would want the following information from the researcher:
  + Please prepare a risk/benefit table in order to assist the Committee decision making.
  + Please clarify the number of Māori participants and the steps that have been taken to contact them. The Committee noted that it would be desirable if there were some Māori participants as Down syndrome is a serious issue for Māori
  + Please clarify whether the drug will be available to participants at the end of the trial and what arrangement the company could come to for future supply for any participants who may derive benefit from it. If it will not be made available to participants this should be clearly stated in the information sheet.
  + Please confirm what follow up will take place if participants experience side effects from taking the study drug.
  + Please provide a list of the other countries in which ethics approval has been applied for and the status of these applications
  + The Committee considers the number of PIS’s confusing. It agrees with the concept of the simplified pictorial PIS but please review with respect to further simplifying the language used. One detailed PIS for guardian/caregivers should be sufficient with simplified attachments for the three consent forms.
  + Please include in the opening paragraph of the PIS that this study is for an experimental drug that has not been used on many human participants so the full extent of side effects are unknown.
  + Please include in the PIS risks associated with increased suicidality.
  + The Committee needs to know about recruitment at all centres and expects the coordinating investigator to be able to report back about this.
  + Please ensure that section on pregnancy in PIS is worded appropriately to the level of understanding of the parent/caregiver.
  + Please clarify 1) Does the drug only work when the patient is taking it? 2) Would there be any adverse effect when the patient discontinues 3) What would be the risk for adverse events of being on the drug long term?
  + Please justify why biobanking is necessary.

Decision

This application was *deferred* pending legal advice on issues relating to consent.

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| **4** | **Ethics ref:** | **14/NTA/11** |
|  | Title: | IFOOD |
|  | Principal Investigator: | Mrs Katrina Pace |
|  | Sponsor: |  |
|  | Clock Start Date: | 30 January 2014 |

Mrs Katrina Pace was present in person and Ms Kathryn Beck and Ms Rozanne Kruger 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.

Summary of ethical issues

The main ethical issues considered by the Committee were as follows.

* Mrs Pace said a number of patients had been asking about the 5:2 diet and that this study is for researchers to establish whether the diet is safe for those on insulin. Mrs Pace advised that they are doing this study on those who require insulin as if it works on those with higher risk of hypoglycaemia it would work on others who do not require insulin.
* The Committee asked for clarification on how standard treatment would be withheld. Mrs Pace confirmed that it would not be normal advice for patients to fast. As the standard treatment is portion control, the withholding of treatment is based on the two day fasting element of the diet.
* Mrs Pace advised that patients were likely to achieve a calorie deficit similar to portion control and this would normally result in a weight loss of about three to five kilograms.
* The Committee advised that the risks for the study, for example hypoglycaemia, should be included in the PIS.
* The Committee asked what the possibility of this being a fad diet was. Mrs Pace advised that there is always the risk of using a fad diet but that there is some evidence on this diet so it is worth investigating.
* Mrs Pace noted that they would be ignoring other factors relating to weight loss, such as exercise and women’s hormones. She confirmed that she was happy with the sample size of 40
* The Committee asked if this research was for Mrs Pace’s Massey University thesis or for the benefit of the DHB. Mrs Pace confirmed that the study was conceived by the DHB and that they are paying for her to do the research. This will also be used for her thesis.
* The Committee asked what processes would be in place to manage risks for participants at home, for example hypoglycaemia. Mrs Pace confirmed that participants will have come through the diabetes centre so they will have a good baseline knowledge of managing these events. They will also have access to diabetes nurses and doctors for this project.
* The Committee asked if there was enough known about the 5:2 diet to ensure that it does not have the effects of other diets, such as rapid weight gain, when the diet ends. Mrs Pace advised that there have been two papers from Manchester which looks specifically at the 5:2 diet rather one day of fasting and one day off. These showed that the risks of the 5:2 diet is lower than for a six-month low calorie diet (of around 500 to 800 calories). She noted that the 5:2 diet promotes healthy eating on the non-fasting days, which makes it easier to integrate into a patient’s lifestyle when the study is completed.

Decision

This application was *approved* by consensus

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| **5** | **Ethics ref:** | **14/NTA/12** |
|  | Title: | IBS Discomfort Elimination Assessment (IDEA) Study |
|  | Principal Investigator: | Dr Alasdair Patrick |
|  | Sponsor: | Vital Food Processors Ltd (New Zealand) (NZ Busine |
|  | Clock Start Date: | 30 January 2014 |

Dr Alasdair Patrick and Mrs Catherine Howie 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 ethical issues

The main ethical issues considered by the Committee were as follows.

* The Committee asked for clarification on the trial procedures. Dr Patrick advised that the study would be recruited to from his private medical practice in Central Auckland. A research nurse who works at Middlemore Hospital for CCREP will come to the central location to see the patients, administer questionnaires and do blood pressure and blood tests.
* Dr Patrick confirmed that the Central Auckland clinic is private and that there would be no doctor’s costs for the visits for participants.
* The Committee asked who would be doing the recruiting. Dr Patrick advised that once people were identified who may be appropriate, they would come to a screening session. He noted that these patients were more likely to be through the private system many patients with IBS symptoms do not get seen through the public system.
* Dr Patrick noted that it would be doctors in the private system who would consent the patients.
* The Committee noted that the protocol was tailored toward the Australian system, particularly in relation to data safety, page 37, table 17.1. Please refer to pages 45 and 46 of the *Standard Operating Procedures for Health and Disability Ethics Committees* for safety reporting. The Committee advised that for New Zealand patients, the investigator should follow New Zealand requirements for annual safety reports, reporting of urgent safety measures and temporary halts. Mrs Howie confirmed that she would discuss this with the sponsor and that the protocol may need to be amended.
* Mrs Howie confirmed that they were still waiting for SCOTT approval.
* The Committee asked for clarification from the sponsor on reporting of negative results.
* The Committee noted there was no option on the PIS for patients to receive results if requested by them.
* The Committee asked for clarification on Māori consultation. Mrs Howie confirmed that she discussed the application with Karla Rika-Heke at Middlemore Hospital who believed that Māori consultation was not required given the low risk nature of the trial, the population being recruited and that there was no tissue sampling. Mrs Howie advised that she would ask for a letter confirming this.
* The Committee noted the discrepancy between answers to P.4.1, which states that there is no specific data available for Māori and P.4.2 which identifies no cultural issues for Māori.
* The Committee asked what the standard treatment for IBS patients would be if they had problems with the study drug. Dr Patrick explained that patients generally came to see him as they were already on another drug which was not working. The standard treatment would therefore be to go back to what they were previously taking.
* The Committee asked how the potential of coercion or conflict of interesting in having Dr Patrick as treating physician would be addressed. Dr Patrick explained that he would be open with participants that they did not need to take part in the study and that they would not be disadvantaged by not taking part.

Decision

This application was *approved* by consensus subject to the following non-standard conditions.

* Please provide a letter of evidence that Māori consultation is not required *(Ethical Guidelines for Intervention Studies, para 4.9).*
* Please provide evidence of SCOTT review (*Ethical Guidelines for Intervention Studies, para 5.51).*

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| **6** | **Ethics ref:** | **14/NTA/13** |
|  | Title: | Wellbeing group for children |
|  | Principal Investigator: | Mrs Emma (Ema) Tokolahi |
|  | Sponsor: |  |
|  | Clock Start Date: | 30 January 2014 |

Mrs Ema Tokolahi and Ms Claire Hocking 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 ethical issues

The main ethical issues considered by the Committee were as follows.

* This study is a wellbeing group for intermediate students and will be evaluated using a cluster randomised control trial. At each school there will be one study arm of either an intervention or a waitlist. The intervention group will be an eight week, one hour per week programme. Those in the waitlist will attend class as normal. Both groups will complete the baseline measures at the beginning and end of the eight weeks. The waitlist group will be told that they are in the waitlist group after completing the first set of measures and will be offered the intervention in the next term.
* Mrs Tokolahi confirmed that the student will assent and the parents will consent to this study. The parents will be consenting to their child taking part and for them to fill out information about their child. The Committee asked whether the parents also needed to consent to completing the questionnaire but agreed that completing a questionnaire is implied consent.
* The Committee asked if teachers would choose which students would participate. Ms Tokolahi confirmed that teachers would nominate children who they believed would benefit from the study but other children could also take part if they expressed an interest.
* The Committee asked about the risk of stigmatisation to children. Mrs Tokolahi explained that this would be addressed by including one or two children identified as role models within the group. The group would not be labelled, instead it would be described as a group that would help with emotions.
* The Committee asked how these role models would be screened. Mrs Tokolahi advised that participants would need to score under 30 in the screening assessment. If they score over 30, they would be referred to secondary services. It is assumed that the role models will score under 30 in the assessment.
* The Committee recommended using a study ID system rather than participant names as at present, there is room for participants to fill in their names.
* The Committee asked what safety procedures would be in place to protect students and the researcher. Mrs Tokolahi confirmed that this would be managed in the same way as clinical practice, i.e. by validating children’s emotions and ensuring safety plans are in place. Ministry of Education protocols are in place if abuse is reported. Mrs Tokolahi advised that she has a clinical supervisor and a supervisor at AUT to support her.
* The Committee asked what would be done to minimise the risk of children passing on information to people outside the group. Mrs Tokolahi explained that there would be a discussion on confidentiality and that children could discuss what they said with others outside the group but not what other people have said.
* The Committee asked for clarification of “adverse event” as referred to in the application. Mrs Tokolahi explained that this was a term for events such as disclosures, physical accident and highly distressed children.
* The Committee asked for clarification on referral to secondary services. Mrs Tokolahi advised that this may occur if something of concern comes up in the group or if a child scores above 30 in the screening assessment. This will be discussed with the child’s parents and a decision will be made by them on whether the referral will take place.
* Mrs Tokolahi explained that the study had been designed by and her and was based on components from her masters’ thesis research in a secondary setting, from her private practice, consultation with a panel of experts, parents of children in private practice and Māori cultural advisors. The Committee asked for a letter of support from the Māori cultural advisors
* The Committee queried what data safety was in place. Mrs Tokolahi explained that in order for the questionnaires to be blinded, she was unable to look at them, but that research assistants would be monitoring them. There would also be a psychologist at AUT assessing the questionnaires and there would be clinical input if worsening symptoms were identified in the second questionnaire.
* The following changes were requested to the PIS and consent form:
  + Please add the words “provided this is done with the consent of the parent/caregiver and child” to the sentence “I agree to the research staff collecting and processing my information” on all consent forms.
  + Please clarify in the PIS what the child and parent/caregiver are being asked to do for this study.
  + Please clarify the role of the teachers and schools, in opening paragraph of PIS.
  + Please include in the PIS for students that parents may have access to their questionnaires if they ask for them.
  + Please include in the consent form for students that they will not share other student’s information outside the group.
  + Please include in the PIS that there is a control group, that both groups will get the intervention but that it may not be until the next term.
  + To avoid stigmatisation, please include information in the PIS on why children will benefit from this group.
  + Please include in the PIS that children may be referred to secondary services if they score over 30 in their screening assessment or if areas of concern are identified in the group.
  + To protect patient confidentiality, questionnaires should use a study ID. Please remove the space in the questionnaires to record participant names.

Decision

This application was *approved* by consensus subject to the following non-standard approval conditions being met.

* Please amend the PIS and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies, para 6.22).*
* Please provide a letter of evidence that Māori consultation has taken place *(Ethical Guidelines for Intervention Studies, para 4.9).*

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| **7** | **Ethics ref:** | **14/NTA/16** |
|  | Title: | Alios BioPharma ALS-8176-503 |
|  | Principal Investigator: | Dr. Thorsten Stanley |
|  | Sponsor: | inVentiv Health Clinical Australia Pty Ltd |
|  | Clock Start Date: | 30 January 2014 |

No researchers were present for discussion of this application.

Potential conflicts of interest

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

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

Summary of ethical issues

The main ethical issues considered by the Committee were as follows.

* The Committee noted this is a First-in-Infant study.
* The Committee were concerned that it was unclear as to whether the study design took into account questions raised by the MHRA, particularly in relation to the statement “It is suggested that the Company obtains at least some safety and PK data with the starting dose in a mini-cohort aged at least 6 months before progressing to the same in the 2 - < 6 months age group and then in infants aged from 4 weeks to < 2 months”.
* In view of the uncertainty surrounding the responses to the MHRA suggestions, The Committee wishes to know if there was an independent peer review which considered the responses from MHRA. As this is a first in infant study, the Committee believes a rigorous peer review is required.
* The Committee asked for clarification on the dosage as this was not clear in the PIS.
* The Committee believed that it was unclear in the PIS whether this is a Phase I and Phase 2 trial and advised that they were unable to approve a multi-dose study where there is uncertainty about the dosing regimes
* The Committee queried why this study is not split into separate projects. Surely if the suggestions of the MHRA are taken into account the first study would be safety and PK data collections on infants at least 6 months old, then a study on >2<6 months, before progressing to the 4 week to 2 month group. The Committee will not consider a multi-dosage, complex design which is First-In-Infant.
* The Committee asked for information on what other countries had applied for ethical approval and the status of these applications.
* The Committee asked for clarification on the data monitoring procedures (R.1.4).
* The Committee asked for clarification on how the risk of coercion would be addressed (R.5.4.1)
* The Committee asked for clarification on what potentially identifiable information would be stored after the study had finished (R.4.2.1).
* The Committee noted that the earlier studies on animals showed reductions in red blood cells but the application is silent on red blood counts on human volunteers in the first trial. Surely this could be a major issue for infants? Please ensure that there is full disclosure of such information in the PIS.
* The Committee advised that data needs to be kept for 10 years after the child turns 16.
* The Committee suggested in future the CI be available for at least a teleconference call when the Committee is addressing such a study involving First-In-Infants
* The following changes were requested to the PIS and consent form:
  + Please prepare a PIS that clearly reflects the multi-stage, different dosage sequences
  + Please include on page 1 of the PIS that there have been no studies of this drug on infants.
  + Please clarify whether tissue samples will be destroyed or the length of time they will be kept.
  + Please include in the PIS that the patient has a 25% chance of receiving a placebo.

Decision

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

* The Committee believed that the study design did not take into account the comments raised by the MHRA *(Ethical Guidelines for Intervention Studies, para 5.4).*

## 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:** | 11 March 2014, 01:00 PM |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

No members tendered apologies for this meeting.

The meeting closed at 5.00pm