|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Committee:** | | Northern A Health and Disability Ethics Committee | | |
| **Meeting date:** | | 21st June 2022 | | |
| **Zoom details:** | | <https://mohnz.zoom.us/j/9481145912> | | |
| **Time** | **Review Reference** | | **Project Title** | **Coordinating Investigator** | | **Lead Reviewers** |
| 12:30pm - 1:00pm | 2022 FULL 12644 | | A study to evaluate the safety and effectiveness of cotadutide given by subcutaneous injection in adult participants with non-cirrhotic non-alcoholic steatohepatitis with fibrosis | Dr David Orr | | Dr Andrea Forde & Ms Catherine Garvey |
| 1:00pm - 1:30pm | 2022 FULL 12058 | | Telehealth-delivered supports for enhancing the social communication of autistic children and caregiver wellbeing | Associate Professor Laurie McLay | | Ms Jade Scott & Mr Jonathan Darby |
| 1:30pm - 2:00pm | 2022 FULL 12365 | | Marae Based Colposcopy | Dr Judy Ormandy | | Dr Sotera Catapang & Ms Catherine Garvey |
|  |  | | *Break (20 minutes)* |  | |  |
| 2:20pm – 2:40pm | 2022 FULL 12382 | | Master Screening Study to Determine Biomarker Status and Potential Trial Eligibility for Patients with Malignant Tumours | Dr Laird Cameron | | Dr Kate Parker & Dr Leonie Parker |
| 2:40pm - 3:00pm | 2022 FULL 12515 | | A Phase I-III study evaluating the efficacy and safety of multiple therapies in cohorts of patients selected according to biomarker status, with stage III NSCLC | Dr Laird Cameron | | Dr Kate Parker & Dr Leonie Parker |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Karen Bartholomew | Non-lay (Intervention studies) | 18/07/2016 | 18/07/2019 | Present |
| Dr Kate Parker | Non-lay (Observational studies) | 11/02/2020 | 11/02/2023 | Present |
| Dr Andrea Forde | Non-lay (Intervention studies) | 22/12/2021 | 22/12/2024 | Present |
| Ms Catherine Garvey | Lay (the Law) | 19/03/2019 | 19/03/2022 | Present |
| Dr Sotera Catapang | Non-lay (Observational studies) | 11/02/2020 | 11/02/2023 | Present |
| Mr Jonathan Darby | Lay (the Law/Ethical and Moral reasoning) | 13/08/2021 | 13/08/2024 | Present |
| Dr Leonie Walker | Lay (Ethical/Moral reasoning) | 13/08/2021 | 13/08/2024 | Present |
| Ms Jade Scott | Non-lay (Intervention/Observational studies) | 15/08/2021 | 15/08/2024 | 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 17th May were confirmed.

## New applications

|  |  |  |
| --- | --- | --- |
| **1** | **Ethics ref:** | **2022 FULL 12644** |
|  | Title: | A study to evaluate the safety and effectiveness of cotadutide  given by subcutaneous injection in adult participants with noncirrhotic non-alcoholic steatohepatitis with fibrosis |
|  | Principal Investigator: | Dr David Orr |
|  | Sponsor: | AstraZeneca Pty Ltd |
|  | Clock Start Date: | 9th June 2022 |

Duncan Hui, Sudha Shankar, Ashwini Mallappa and Lisa Cowan were present via videoconference 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 resolved ethical issues

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

1. The Committee clarified that the dosage periods were appropriate given the inquisition into the maximal efficacy of the drug in one cohort over 84 weeks.

Summary of outstanding ethical issues

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

1. The Committee raised that Participants in Part A will not be enrolled in the trial for the 'max benefit' period described in Protocol 4.2.2 and that the protocol specifically excludes their enrolment into Part B. The Committee noted that it is expected that Participants receiving a therapeutic benefit in Part A will be able to have continued access to the drug. The Researcher explained that there would be a possibility for Participants in Part A to access a further 36-week period until the last Participant has completed their treatment. The Committee noted that this is not clear in the study protocol and requested that this is confirmed with the study sponsor to ensure the study meets National Ethical Standards for Health and Disability Research and Quality Improvemen*t,* para 10.15 – 10.17.
2. The Committee also noted that the research also includes the evaluation of an AI, currently not licensed by the FDA, for histopathology.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

1. Please include more information on how participant’s data will be used (i.e., AI research).
2. Please include a reference to Standing Committee on Therapeutic Trials (SCOTT) approval.
3. Please ensure Participants are supplied with further information about the biobank.
4. Please include explain whether historical data can be used from the screening biopsy, and why this information may be required.
5. Please provide more information on where genetic samples will be stored (names of biobanks and locations).
6. In the optional PIS, please change the headings from black on blue to white on blue for accessibility.
7. Please review the Participant-facing documents for spelling mistakes (i.e., macrons on te reo words).

**Decision**

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

1. Please address all outstanding ethical issues, providing the information requested by the Committee.
2. Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
3. Please update the study protocol, taking into account the feedback provided by the Committee. (National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).

After receipt of the information requested by the Committee, a final decision on the application will be made by Dr Andrea Forde & Ms Catherine Garvey.

|  |  |  |
| --- | --- | --- |
| **2** | **Ethics ref:** | **2022 FULL 12058** |
|  | Title: | Telehealth-delivered supports for enhancing the social  communication of autistic children and caregiver wellbeing |
|  | Principal Investigator: | Associate Professor Laurie McLay |
|  | Sponsor: | University of Canterbury |
|  | Clock Start Date: | 9th June 2022 |

Dr Jenna van Deurs was present via videoconference 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 resolved ethical issues

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

1. The Committee asked for more information on the programmes being used in the study and whether these programmes are already in use in the intended target populations. The Researcher confirmed that these are common interventions in New Zealand and internationally for a wide range of health issues, including in autistic children.
   1. The Committee noted the studies use of the Whaiora Tamariki programmes (Caregiver Acceptance and Commitment Therapy - ACT and Naturalistic Developmental Behavioural Interventions – NDBI) and asked whether they have been designed to be delivered as a web-based programme. The Researcher explained that they were initially designed to be in-person, however other studies on the efficacy the web-based version suggest that the programmes are effective online. The researcher explained the three cohorts are designed to test the efficacy of the web-based groups.
   2. The Committee noted the substantial time commitment expected for those in the third cohort (who will be involved in the combined ACT and NDBI). The researcher acknowledged the time commitment for the third cohort. To mitigate this, the Researcher explained that they will be transparent with expected time commitments per module so that participants are aware and manage their time appropriately.

Summary of outstanding ethical issues

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

1. The Committee requested more information be added to the study protocol on the design and consent process.
   1. Please include the statement on returning consents via email or post.
2. The Committee noted that the study protocol states ‘non-autistic caregivers’ would be involved in the study, however it is mentioned in the screening document that both non-autistic and autistic caregivers would be included in the study. Please amend and ensure this is consistent across documents.
   1. The Committee raised that if the study aims to include the perspectives of autistic and non-autistic caregivers, please create a consent form designed for these groups and submit to the Committee for review.
3. The Committee requested that if concerns are raised in the survey (i.e., distress) that the participant is contacted within 24 hours instead of stating ‘in a timely manner’.
4. The Committee raised that the study documentation states that the study will specifically target Pasifika participants. The Committee noted that the participant-facing documentation will be in English, however the consent form states that participants will need to confirm that they have had information read to them in their ‘first language’. Please ensure that the information is consistent and provide details on what translation options are available.
5. The Committee noted that the study will include children who have been formally diagnosed with autism, as well as children with a ‘high-likelihood’ of being diagnosed with autism. The Committee asked for more information on the screening process to identify those in the latter group. The Researcher explained that there is a formal screening tool which will be utilised by the study team, and they will have received formal training in the screening process. The Committee requested that this information be provided for review by the Committee.
6. The Committee noted the daily surveys referenced in the study documents and requested that these are submitted for review.
7. The Committee inquired whether the suggestions made in the study peer review had been incorporated. The Researcher outlined the points raised in the peer review and confirmed that the suggestions had been integrated into the study.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

1. Please provide more information on the video samples (how many, how long the videos need to be, etc).
2. Please specify the total time the questionnaires will take.
3. Please include the other participants in the group sessions as those who will have access to identifiable information.
4. Please ensure that data is kept for 10 years after the youngest participant has turned 16 years old (*National Ethical Standards for Health and Disability Research and Quality Improvement, para 6.28*). Please ensure this is reflected in the study protocol.
5. Please include a section on who is funding the study.
6. Please inform participants that they will have ongoing access to the modules once the study has concluded.
7. Please include the expected time commitment and ethics reference in the study advertisement.
8. Please clearly explain that the study will be exploring the experiences both non-autistic and autistic caregivers. Please ensure that it is clearly stated that autistic caregivers can opt-out from being included in the study group.
9. Please review the participant-facing documents and include more lay-friendly language. Please also ensure that these documents are discussed with participants to ensure they comprehend the information provided prior to consenting.

ASSENT FORM

1. Please consider including more images to help aid understanding.

**Decision**

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

1. Please address all outstanding ethical issues, providing the information requested by the Committee.
2. Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
3. Please update the study protocol, taking into account the feedback provided by the Committee. (National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).

After receipt of the information requested by the Committee, a final decision on the application will be made by Mr Jonathan Darby & Ms Jade Scott.

|  |  |  |
| --- | --- | --- |
| **3** | **Ethics ref:** | **2022 FULL 12365** |
|  | Title: | Marae Based Colposcopy |
|  | Principal Investigator: | Dr Judy Ormandy |
|  | Sponsor: | C&CDHB |
|  | Clock Start Date: | 10th June 2023 |

Judy Ormandy and Sara Filoche were present via videoconference 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 resolved ethical issues

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

1. The Committee clarified with the Researchers that the study colposcopist will conduct the colposcopies at the marae-based hauora health clinic site, however there may be another colposcopist who will conduct the procedure if the participant selects to have the colposcopy in the usual clinical setting (i.e., in the hospital clinic). The Researcher clarified that the interviews will be conducted by a research assistant.
   1. The Committee asked how Participants will be recruited into the study and select the marae-based care. The Researcher explained that information regarding the study and choice of site will be shared by General Practitioners and the colposcopy nurse at the time of referral and the making of the colposcopy appointment.
2. The Researchers assured the Committee that setting up the procedure in the marae-based clinic will provide a safe and similar standard of care as the hospital setting (and is utilising equipment that is designed to be portable). However, if there are clinical or technical reasons that the procedure cannot be carried out in the marae clinic, the participant will be referred to Wellington hospital. The researcher confirmed that where potential difficulties were anticipated at the time of booking, then such participants would be seen at the hospital clinic.
3. The Committee asked whether the procedure will be a screening or diagnostic colposcopy. The Researcher clarified that it will be a diagnostic colposcopy.

Summary of outstanding ethical issues

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

1. The Researchers explained that participants may request to have the colposcopy in Wellington hospital. The Committee suggested that the Researchers take note of the reasons why participants may request to not attend the marae-based clinic as this will help inform their study outcomes.
   1. Please also clarify the qualifications of the other colposcopist who will conduct the procedure in the marae-based clinic if it is not the usual colposcopist from Wellington Hospital.
   2. Please provide information on how the procedure across different colposcopist’s are the same to ensure the intervention is consistent and provide the same results.
2. Please clarify if all those who have an abnormal screening result will be included in the study.
3. Please clarify that this study is a qualitative study and what this means to the study outcomes. As this is a descriptive qualitative study, please remove ‘Due to sample size, there will be insufficient power to detect statistically significant differences’.
4. The Committee requested that the letter to GPs be uploaded for Committee review.
5. The Committee requested that the privacy agreement between the research team and transcription service be uploaded for Committee review.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

1. Please include more information on why the participant is being invited to take part in the study and details on the colposcopy (i.e., the participant has had an abnormal cervical smear).
2. Please explain why participants are provided with the transcript of the interview (i.e. for general information, or whether they are able to request changes to the transcript). Please also ensure that personal identifiable information will be removed from the videos prior to being sent to the transcribing service.
3. Please specify the location of the marae clinic early in the information sheet.
4. Please include a statement that informs the participant that there is a chance they may be referred to Wellington hospital if the colposcopy is unable to be completed.
5. Please include information on who will conduct the study interviews and if they are the only interviewer since semi-structured questionnaire is used (to avoid diversity of question/s)
6. Please review the document for any spelling or grammar mistakes (i.e., ‘we would like to find out from wahine about their experience and views marae-based colposcopy services’).
7. Change Southern HDEC to Northern A HDEC as the approving ethics committee.

**Decision**

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

1. Please address all outstanding ethical issues, providing the information requested by the Committee.
2. Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
3. Please update the study protocol, taking into account the feedback provided by the Committee. (National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).

After receipt of the information requested by the Committee, a final decision on the application will be made by Ms Catherine Garvey & Dr Sotera Catapang.

|  |  |  |
| --- | --- | --- |
| **4** | **Ethics ref:** | **2022 FULL 12382** |
|  | Title: | Master Screening Study to Determine Biomarker Status and  Potential Trial Eligibility for Patients with Malignant Tumours |
|  | Principal Investigator: | Dr Laird Cameron |
|  | Sponsor: | Roche Products (New Zealand) Limited |
|  | Clock Start Date: | 10th June 2022 |

Dr Laird Cameron and Ms Vivian Sun was present via videoconference 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 Kate Parker declared a potential conflict of interest due to working with Dr Cameron in the past. Dr Parker is not involved or interest in the outcome of the applications before the Committee (2022 FULL 12382 & 2022 FULL 12515). The Committee agreed that there is no conflict of interest.

Summary of resolved ethical issues

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

1. The Committee noted that there is repetition between the master screening study and the second study. The Committee asked why this was the case and whether it was necessary for Participants to be screened twice. The Researcher explained that the master screening study would be offered to all participants prior to starting chemotherapy or radiation treatment; a small percentage of those screened will return results which will allow them to be considered for the second study which will offer targeted treatments. The screening in the intervention study considers the response to chemotherapy or radiation therapy, which would not have begun at the time of the first screening in the master study.
   1. The Researcher confirmed to the Committee that if a participant does not return results which would allow them to take part in the study, the master screening process may lead to off-trial treatment options.
2. The Committee asked for more information on the recruitment process. The Researcher explained that the participants would be recruited by the study team through clinics where the participants would be treated.
   1. The Committee asked whether there was a risk of coercion due to the participants being recruited by their treating clinician. The Researcher explained that their trials are always optional to participants and they take care to ensure participants know that there is no obligation to take part. It is communicated to the Participant that the decision to not take part in the trial does not influence their usual standard of care.
3. The Committee noted the length of the study, commenting that it seems longer than usual for a screening study (8 months). The Researcher explained that there will be one month for the screening process and returning the results, with a 6 month follow up to ascertain what treatment participants are receiving.
4. The Committee noted the high rates of Māori who are diagnosed with lung cancer and the risk of a widening knowledge gap due to under-representation of Māori in clinical studies. The Researcher explained that the study will focus on anyone that fits the eligibility criteria and would do their best to meet cultural needs as they are met. The research study nurse is Māori with good knowledge of Māori customs and would support any Māori participants. For future studies, the Researcher is establishing a Māori support group.

Summary of outstanding ethical issues

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

1. Please provide a New Zealand-specific insurance certificate.
2. The Committee noted the statement “the results from the biomarker testing may enable you to participate in a Roche research study in the future". Please ensure that if Roche does not have a trial that would relate to the identified biomarker that other trials from other sponsors or research be suggested.
3. The Committee noted in the Data Management Plan that some parts are not relevant to this trial (section 8 and the reference to 7.4 and 7.5). Please review and amend.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

1. Please change the statement ‘you may be reimbursed for travel’ to ‘you will be reimbursed for travel’, as this is not optional.
2. Please replace ‘race’ with ‘ethnicity’.
3. Please ensure there is a participant status check prior to conducting the 6-month follow up phone call.
4. Please outline which genes will need to be affected for eligibility in the study. Please make a note that other genes will also be tested.
5. Please be clear on whether any incidental findings (i.e., genetically inherited changes) will be communicated with participants.
6. Please remove reference to teaspoons for measurements of blood and replace with millilitres.

OPTIONAL PIS

1. Please ensure there is a location listed for all laboratories.
2. Please clarify for participants that the optional storage is not a study itself, however it may be used in future research.
3. Please refer to the tissue bank rather than the study.
4. Please clarify how long tissue will be kept for, and ensure this is consistent across study documents.

**Decision**

This application was *approved* with *non-standard conditions* by consensus, subject to the following non-standard conditions:

* please address all outstanding ethical issues raised by the Committee
* please update the Participant Information Sheet and Consent Form, taking into account the feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
* please update the study protocol, taking into account the feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).*

|  |  |  |
| --- | --- | --- |
| **5** | **Ethics ref:** | **2022 FULL 12515** |
|  | Title: | A Phase I-III study evaluating the efficacy and safety of  multiple therapies in cohorts of patients selected according to biomarker status, with stage III NSCLC |
|  | Principal Investigator: | Dr Laird Cameron |
|  | Sponsor: | Roche Products (New Zealand) Limited |
|  | Clock Start Date: | 10th June 2022 |

Dr Laird Cameron and Ms Vivian Sun was present via videoconference 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 Kate Parker declared a potential conflict of interest due to working with Dr Cameron. The Committee were satisfied that Dr Parker is not conflicted in relation to the applications before the Committee. (2022 FULL 12382 & 2022 FULL 12515).

Summary of resolved ethical issues

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

1. The Committee asked for more information on the recruitment process. The Researcher explained that the participants would be recruited by the study team through clinics where the participants are receiving treatment.
   1. The Committee asked whether there was a risk of coercion due to the participants being recruited where the investigators are part of their treating team. The Researcher explained that their trials are always optional to participants and there is no obligation to taking part. It is communicated to the Participant that the decision to not take part in the trial does not influence their usual standard of care.
2. The Committee noted that there are three parts to the study, depending on which mutation the participant has. The Committee asked whether participants would have the ability to switch to the study drug if they are not responding to durvalumab. The Researcher explained that this would not be possible due to a lack of evidence that suggests durvalumab would be appropriate in this evaluation setting. If the Participant was not responding to the study drug, they would be removed from the study and placed on other approved medications.
3. The Committee asked why participants are being asked to fill out another Future Unspecified Research (FUR) consent form when they have given consent for FUR in the previous (Master Screening - 2022 FULL 12382) study. The Researcher responded that there would be additional tissue taken that would not have been required in the previous study, and so this would require reconsenting to FUR by participants.
4. The Committee asked for more information on the interactive (voice- or web-based) response system mentioned in the study protocol. The Researcher explained that it is a voice recognition software that ensures the randomisation is independent.
5. The Committee noted the high rates of Māori who are diagnosed with lung cancer and the risk of a widening knowledge gap due to under-representation of Māori in clinical studies. The Researcher explained that the study will focus on anyone that fits the eligibility criteria and would do their best to meet cultural needs as they are met. The research study nurse is Māori with good knowledge of Māori customs and would support any Māori participants. For future studies, the Researcher is establishing a Māori support group.

Summary of outstanding ethical issues

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

1. The Committee noted that the study protocol mentions at-home health visits, however these are not being conducted in New Zealand. Please amend and remove if it is not an option in New Zealand.
2. The Committee raised that the protocol refers to other ways that participants may be recruited into the trial outside of the master screening study. The Researcher explained that through the testing of some biomarkers (i.e., anaplastic lymphoma kinase – ALK) participants may be able to enter the study without being involved in the master screening study. The Researcher stated that this would be clarified with the study sponsor and clarification provided in the PIS and Protocol accordingly.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

1. Please change the statement ‘you may be reimbursed for travel’ to ‘you will be reimbursed for travel’, as this is not optional.
2. Please replace ‘race’ with ‘ethnicity’.
3. Please mention the possibility of a positron emission tomography (PET) scan in the main PIS in addition to the PET PIS. Please also provide more information on why a PET scan may be needed.
4. The Committee notes in the study protocol the sponsor states that “retaining data and tissue for those who are screened and not eligible, including using samples for future research”. The Committee requested that this is made clearer in the PIS for those who are not eligible for the study and provide an option to withdraw their data and tissue from being used.
5. Please provide a statement informing the participants that the study has SCOTT approval.
6. Please clearly explain what durvalumab is in lay language.
7. Please clearly outline why the study drugs will not be available after the trial.
8. Please clearly explain that no incidental findings are fed back from genome testing.
9. Please highlight the need to fill in the medication diary to participants.
10. Please remove reference to teaspoons for measurements of blood and replace with millilitres.

**Decision**

This application was *approved with non-standard conditions* by consensus, subject to the following non-standard conditions:

* please address all outstanding ethical issues raised by the Committee
* please update the Participant Information Sheet and Consent Form, taking into account the feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
* please update the study protocol, taking into account the feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).*

## General business

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

|  |  |
| --- | --- |
| **Meeting date:** | 19 July 2022 |
| **Zoom details:** | https://mohnz.zoom.us/j/9481145912 |

1. **Review of Last Minutes**

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

1. **Matters Arising**
2. **Other business**
3. **Other business for information**
4. **Any other business**

The meeting closed at 4:00pm.