DATA AND BACTERIAL ISOLATE MANAGEMENT PLAN

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Protocol: RandOmised Arthroplasty infection worlDwide Multidomain Adaptive Platform trial (ROADMAP)

Sponsor: University of Newcastle/Aotearoa Clinical Trials

Site: Te Whatu Ora localities

Co-ordinating Investigator: Thomas Hills

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1 INTRODUCTION

This Data and Bacterial Isolate Management Guide outlines how data and bacterial isolates will be handled during the study RandOmised Arthroplasty infection worlDwide Multidomain Adaptive Platform trial (ROADMAP) and after its completion.

2 STUDY STRUCTURE

Details of the personnel and organisations responsible for trial conduct are shown in the Core Protocol and the New Zealand Region-Specific Appendix. The New Zealand Sponsor is the Aotearoa Clinical Trials, and the Co-ordinating Investigator is Dr Thomas Hills, Te Toka Tumai, Auckland, New Zealand. The study structure is outlined in Table 1.

TABLE 1. STUDY STRUCTURE

Sponsor	1. Hunter Medical Research Institute (Global Sponsor) John Hunter Hospital, Lot 1 Kookaburra Cct, New Lambton Heights, NSW 2305, Australia NSW 2308 2. Aotearoa Clinical Trials (New Zealand Sponsor) 100 Hospital Road, Papatoetoe, Auckland 2025, New Zealand
Contract Research Organisation	N/A
Lead Site (New Zealand)	Middlemore Hospital 100 Hospital Road, Papatoetoe, Auckland 2025, New Zealand
Co-ordinating Investigator	Thomas Hills 2 Park Road, Grafton, Auckland 1023, New Zealand
New Zealand Laboratory	Middlemore Hospital Microbiology Lab 100 Hospital Road, Papatoetoe, Auckland 2025, New Zealand
Overseas Laboratory	Hunter Medical Research Institute John Hunter Hospital, Lot 1 Kookaburra Circuit, New Lambton Heights, NSW 2305, Australia
Imaging Vendor	N/A

3 ORGANISATIONAL DATA GOVERNANCE OVERSIGHT

The following institutional data policies apply for the Study:

- Health research and privacy: Guidance notes for health researchers and ethics committees (Health Research Council of New Zealand).
- Data governance will be in accordance with each site's current policies/SOPs.

4 Consent for Data and Bacterial Isolate Collection and Use

The ROADMAP study consists of both 1) an adaptive platform trial where surgical and antibiotic treatments are randomly assigned to identify the optimal management of prosthetic joint infection (PJI) and 2) a linked observational registry that records a smaller amount of data from existing clinical records.

Participants will be informed of, and provide consent for, the collection and use of their data and bacterial isolates for the purposes of the 'platform' component of this study, and for any mandatory secondary uses. Bacterial isolates are cultured as part of usual clinical laboratory diagnostic processes. No human tissue is collected or stored for the study.

A waiver of consent has been granted by the approving HDEC for the study [insert HDEC number] to recruit all eligible patients into the registry component of the trial. In this situation, participants will therefore not be informed of, or consent to, the collection and use of their data for the purposes of the ROADMAP registry. There is no bacterial isolate collection involved with the registry component of the study.

5 Data and Bacterial Isolate Collection

Data will be collected from the following sources:

- Participant medical records (if indicated)
- Study outcome assessment interviews
- Communications with participant's clinical care team (if indicated).
- The National Minimum Dataset, the Medicines Data Repository, and the New Zealand Orthopaedic Association Joint Registry.

No human tissue is being collected for this study. Bacterial isolates will be collected, but do not contain human tissue and are not considered to be a human biospecimen. Bacterial isolates will be collected from the following sources:

- Prosthetic Joint Infection (PJI) samples will only be collected from the participant by the primary hospital clinicians during the study as part of routine hospital care and not specifically for the purposes of the study (identification of bacteria in samples from a prosthetic joint is the most common way a prosthetic joint infection is diagnosed).
- The bacterial isolates grown from the PJI samples will be stored and analysed as part of the study.

Data will be collected primarily by the Investigator or designated study staff. Bacterial isolates will be collected as part of routine clinical care, as clinically indicated, primarily by the primary hospital clinicians. All study personnel involved in data and bacterial isolate collection will be trained in GCP, study protocol, and collection requirements.

Collection of data will be limited to that necessary for the specified purposes of the study, which is to identify the best management of patients with prosthetic joint infections. Any additional collection of data or bacterial isolates for additional purposes will require a study amendment and explicit consent.

6 PRIVACY AND CONFIDENTIALITY

Participants' privacy and confidentiality will be respected through the protection of their data and bacterial isolates as outlined in this plan. The Investigator will comply with legal and regulatory requirements regarding the privacy and confidentiality of participants' data and bacterial isolates.

Participants have the right to access and correct personal data held by the site.

6.1 BREACH OF PRIVACY / CONFIDENTIALITY

A breach of privacy means unauthorised or accidental access to, or disclosure, alteration, loss, or destruction of a participant's information.

In the event participant privacy and confidentiality is breached during the study, the following steps will be taken:

- Action will be taken to reduce the risk of harm following the breach. Where possible, the recipient will be contacted and asked to destroy or return any electronic the disclosed material.
- The participant will be informed of the breach as soon as practicable (unless the participant is under the age of 16 and notification would be contrary to his/her interests; or notification would be likely to prejudice the health of the participant (after consultation with the participant's health practitioner, where practicable), and provided with support as required.
- A site and/or Sponsor (as appropriate) quality review will be conducted to ascertain factors contributing to the breach, and any corrective action required to prevent future breaches.
- The approving HDEC will be informed.
- For notifiable privacy breaches of privacy under the Privacy Act 2020, the New Zealand Privacy Commissioner will be notified in accordance with that Act.

7 FORMS OF DATA AND BACTERIAL ISOLATES

7.1 IDENTIFIABLE DATA AND BACTERIAL ISOLATES

Study data and bacterial isolates will be collected in identifiable form.

Source documents refer to identifiable data collected for the purposes of this study. For the purposes of this data management plan, identifiable data includes the participant's existing medical / clinical records which will constitute the primary source documents for the study.

Study data will generally be entered directly into the electronic CRF (eCRF). While they will be derived from an identifiable form, the data collected in the eCRF will be de-identified.

Source documents will be held at the site in identifiable form.

7.2 De-identified Data and Bacterial Isolates

De-identified data and bacterial isolates in this study includes but is not limited to

- Case Report Forms.
- Bacterial isolates from prosthetic joint infections
- Communications from the site to the Australian Sponsor or overseas laboratory.
- Data generated by the New Zealand/overseas laboratory

De-identified bacterial isolates and data will carry the participant's unique study code. The Investigator will retain a log linking participant code with identifiers. This log will not be made available to the overseas laboratory or Australian Sponsor.

All data and/or bacterial isolates sent to the overseas laboratory or Australian Sponsor will be de-identified. All data generated by these parties will be in de-identified form. No attempt will be made to re-identify participants. Identifiable data required for data linkage will be stored on a separate, secure, password protected platform that will only be accessible to site staff and a central data coordinator in New Zealand. Once the linkage data has been completed and sent to the main study database in Australia, there will be no way to re-identify the data.

7.3 Anonymous / Anonymised Data [and/or Bacterial Isolates].

N/A.

8 Access to and Use of Data and Bacterial Isolates

Collected data and bacterial isolates will be used to answer the research questions and fulfil the study requirements described in the study protocol, and for the secondary purposes outlined in Sections 8.4 and 8.5.

8.1 Identifiable Data and Bacterial Isolates

Identifiable data and/or bacterial isolates may be accessed by the following groups:

- The Investigator and designated study staff, to fulfil protocol requirements.
- A regional data coordinator in New Zealand to facilitate data linkage.
- Local laboratory staff, to process, analyse and report bacterial isolate samples.
- Study monitor(s), for eligibility confirmation and source data verification purposes.
- The New Zealand Sponsor, for audit purposes.
- The New Zealand Sponsor and its authorised representatives, in the event of a compensation claim by a participant.
- The Health and Disability Ethics Committee, for legal and regulatory purposes.
- Health, regulatory, or government agencies, for legal and regulatory purposes.
- The participant's GP or appropriate specialist, to inform them of study participation, and in the event of an incidental finding of potential clinical significance.

- The Medical Office of Health, in the event of a positive result for a notifiable disease.

Rarely, it may be necessary for the Investigator to share identifiable data with people or groups not listed above – for example, in the event of a serious threat to public health or safety, or to the life or health of the participant or another person; or if the data is required for certain legal situations.

8.2 De-identified Data and Bacterial Isolates

De-identified data and bacterial isolates will be accessed and used by the following groups:

- The Investigator and suitably trained and experienced study staff, to conduct the study.
- Sponsor, study monitor(s), for source data verification purposes.
- The overseas laboratory, for sample processing, analysis, and reporting purposes.
- The Sponsor, for study conduct, data analysis and pharmacovigilance purposes, product registration and marketing, or as otherwise permitted by applicable local and international laws and regulations. Third parties working with or for the Sponsor, including the Sponsor's subsidiaries and affiliates and third-party researchers, may also have access for these purposes.
- The Health and Disability Ethics Committee, to comply with legal and regulatory duties.
- Health, regulatory, or government authorities, to comply with legal and regulatory duties.

De-identified bacterial isolates will be used for analyses as described in the protocol and microbiology appendix.

De-identified data may be included in published study results including, but not limited to, peer-reviewed publications, clinical trial registry websites, scientific meetings, and regulatory / marketing submissions.

8.3 Anonymised Data and Bacterial Isolates

N/A.

8.4 Sending of Data and Bacterial Isolates Overseas

De-identified data will be sent overseas to Australia.

De-identified bacterial isolates will be sent to Australia (see Section 2 for details) for analysis and storage.

Participants will be informed of the potential risks and cultural issues associated with sending and storing data and bacterial isolates overseas, although there is New Zealand representation on overseas governance committees which will mitigate this risk, including the Global Trial Steering Committee, the Global Trial Management Group, the Antibiotic Working Groups, the Surgical Working Group, the Registry Working Group, and the Microbiology Working Group.

8.5 Future Use of Data and/or Bacterial Isolates

De-identified and anonymised data and bacterial isolates will be used by the Sponsor for future medical or scientific research as specified below:

- unspecified purposes which are directly related to the study question(s)
- unspecified purposes which are related to the item and/or condition under study

De-identified data and stored bacterial isolates may be made available to other researchers on request for future research as specified above and/or will be added to data from other sources to form larger datasets.

In all cases, the Sponsor must be satisfied that appropriate Data and Bacterial Isolate Management Plans are in place and that ethical approval for use has been obtained in accordance with local laws and regulations.

8.6 Commercial Use of Data and Bacterial Isolates

N/A

8.7 Data Linking

The study will link data obtained from the study and other routinely collected data from a range of databases and registries. This data linking is mandatory for participants.

Details of the planned data linking include:

- The method of linking is deterministic.
- Variables used will be NHI and date of birth. This will be used annually for the duration of the study to link data from the National Minimum Dataset, the Medicines Data Repository, and New Zealand Orthopaedic Association Joint Registry.
- Linking will be undertaken by the regional study coordinators. Aotearoa Clinical Trials will be accountable for the linked data.
- Participants privacy will be protected by allowing only regional study personnel to perform data linkage. As soon as outcome data have been collected, any identifying information is replaced with the trial identifier.
- Participants who are concerned about data linkage should not enrol in the study.
- Bias is mitigated through using the registry and data linkage, as it avoids analysis of trial patients alone, providing information about the generalisability of the ROADMAP trial's findings.
- The Australian trial sponsor will have access to the linked data once it is de-identified to provide a greater quantity and quality of outcome data on the study interventions.
- Security measures include data linking taking place in New Zealand to ensure there is no transfer of identifiable data overseas. As soon as outcome data has been obtained, any identifying information will be replaced with the trial identifier. All identifiable information that will be used for the purpose of data linkage will be stored on a separate, central platform (REDCap) that will only be accessible to site staff, and a central data co-ordinator from the management team in New Zealand. Once linkage data has been sent centrally to Australia, there will be no way to reidentify data.
- Linked datasets will be stored on a central secure RedCap database that will only accessed by the central data coordinator from the management team. The database will have restricted access (password protected), verifiable audit trails and in compliance with all regulations concerning the electronic storage of data. Once linkage data is sent centrally, there will be no way to reidentify the data. The Global Sponsor will be the custodian of the final trial dataset. No-one outside the TMG will be given access to the data without their permission. All information will be kept strictly confidential.

- Following study close out and locking of the database, it will be stored on the servers of the University of Newcastle. All analyses performed and the final data set will be archived together according to the University standard operating procedures. These records will be kept for a minimum of 15 years after the completion of the trial before being destroyed or erased, as per NHMRC guidelines.

8.8 Registry and Biobank

We are not submitting de-identified data to an established registry or data bank.

There is no biobank associated with this study. Bacterial isolates from PJI samples will be collected from the participant and stored as part of routine hospital care.

9 Storage and Destruction of Data

9.1 Identifiable Data and Source Documents

Hospital records (which constitute the identifiable data/source documentation for the study) will be retained in line with local policies and do not fall within the scope of this Plan.

During the study, study-specific source documents will be maintained in password protected computers in locked rooms and password protected databases via password protected computers.

Post-study, study-specific source documents will be archived according to each site's local archiving policies.

Source documents will be retained for at least 15 years, then destroyed by secure destruction as per local guidelines.

The Participant Information Sheet and Consent Form (PISCF) will be retained by the site and a copy of it will form part of the participant's clinical record.

9.2 De-identified Data

Identifiable data will be converted to a de-identified form at the study site, at which point it is entered into electronic case report forms using a secure data platform. The data platform complies with international and national regulatory requirements for electronic data capture systems in the countries where it is used. Data entry will be limited to designated study staff trained and experienced in transcribing data for this purpose.

De-identified data will carry study specific identifiers specific to each individual participant. The Investigator will retain a log linking participant code with identifiers. This log will not be made available to the overseas laboratory or Australian Sponsor.

The de-identified database will remain on Spiral Software (Wellington, New Zealand) servers for up to approximately the duration of the trial. Data will then be archived and stored by the University of Newcastle indefinitely.

De-identified data is stored long-term by the Sponsor in New South Wales, Australia in secure cloud-based servers.

De-identified data will be retained for at least 15 years.

10 Storage and Destruction of Bacterial Isolates

10.1 New Zealand Laboratory

Middlemore Hospital Microbiology laboratory is responsible for the storage, testing/analysis, and destruction of the bacterial isolates collected as part of routine clinical care for this study, described in section 7.1 and 7.2.

Bacterial isolates will be labelled as detailed in Section 7.

Bacterial isolates will be transported to the central New Zealand laboratory by courier. Copies of de-identified samples will be shipped in bulk to Hunter Medical Research Institute in Australia. Copies of the isolates will also remain in NZ in the Middlemore Hospital laboratory under NZ governance. Chain of custody is recorded at all steps.

The laboratory is Good Laboratory Practice (GLP) compliant. The facilities are secure with access to bacterial isolates restricted to those staff directly involved in their analysis.

Bacterial isolates will be retained indefinitely.

10.2 Overseas Laboratory

10.2.1 Bacterial Isolates – Mandatory Research

Bacterial isolates will be labelled as detailed in Section 6.

The isolates, as described in Section 7.3, will be sent in the care of specialised courier companies in compliance with IATA guidance, to the overseas laboratories for the tests/analyses as described in the protocol.

All laboratories where isolates are stored or processed follow GLP principles and are appropriately accredited with the relevant body of the country in which they are located. Laboratory facilities are secure, with bacterial isolate access restricted to those staff directly involved in their analysis.

The following laboratories will be utilised for the current study:

- *Middlemore Hospital Microbiology Laboratory,* 100 Hospital Road, Papatoetoe, Auckland 2025, New Zealand. Bacterial isolates from prosthetic joint infections.
- *Hunter Medical Research Institute,* John Hunter Hospital, Lot 1 Kookaburra Circuit, New Lambton Heights, NSW 2305, Australia. Bacterial isolates from prosthetic joint infections.

Bacterial isolates will be retained indefinitely, then destroyed by local regulatory guidelines. Bacterial isolates collected as part of routine clinical care will be processed according to local laboratory protocols and policy.

10.2.2 Bacterial Isolates – Optional Research

N/A.

11 CONSULTATION

Consultation regarding data and bacterial isolate management will be undertaken with the following relevant communities/stakeholders:

11.1 MĀORI DATA AND BACTERIAL ISOLATE SOVEREIGNTY

During the study, data and bacterial isolates may be collected from participants identifying as Maori. Bacterial isolates will be collected as clinically indicated, not for the purposes of the study but for the purposes of clinical care. Bacterial isolates will be retained and analysed for the study. Taking of human tissue is a major cultural issue for Māori as it is linked to whakapapa and continuation of Māori as a nation. For some Māori, human tissue is considered tapu & imbued with wairua.

Personal and health information is a taonga (treasure) and will be treated accordingly.

Formal Māori consultation for this study will be completed as part of the Locality Approval Process for New Zealand study site(s). Any recommendations for additional measures to improve Māori rights and interests in relation to data and bacterial isolates will be acted upon. We have a Māori Investigator and Māori patient representative who can inform the conduct of ROADMAP in New Zealand.

The principles of whakapapa, whanaungatanga, rangatiratanga, kotahitanga, manaakitanga, and kaitiakitanga are applied in the following ways:

- Health data collected is understood by the study team to be very valuable to the participants and will be handled and analysed with respect.
- Data collected during the study will be stored in a safe secure way which we will continue to review throughout the study to ensure it remains protected.
- All participants data will be used when analysing the results of the study.

12 RETURN OF RESULTS

Participants have the right to request a lay summary of study results.

12.1 INCIDENTAL FINDINGS

In the event that a study assessment returns a result of potential clinical significance, the participant will be informed. The participant's usual doctor and / or an appropriate specialist will be notified, and follow-up will be arranged.

12.2 RESULTS ARISING FROM FUTURE RESEARCH

12.2.1 Data

Results will be made available to participants of any future research conducted using data collected in this study through the ROADMAP website. Participants are informed of this in the PISCF.

12.2.2 Bacterial Isolates

Participants will not be provided with the results of any future research conducted on bacterial isolates collected in this study.

12.2.3 Databank / Registry /Biobank submission

N/A.

13 Withdrawal of Data and/or Bacterial Isolates

Participants may withdraw consent for the collection of data at any time, without providing a reason.

Should a participant withdraw consent, no further data and/or bacterial isolates will be collected by study staff.

Data collected prior to the participant's withdrawal will continue to be used and analysed.

Bacterial isolates collected prior to the participant's withdrawal will not continue to be used and analysed for the purposes of the study.

Bacterial isolates collected and/or stored for future research will be destroyed provided it is still able to be traced.

For withdrawal of data and bacterial isolates submitted to Data Banks, Registries/Biobanks, refer to Section 8.8

APPENDIX

N/A