ROADMAP TRIAL INTEGRITY SUITE: DATA MANAGEMENT PLAN

VERSION 1.0, DATED 22 APRIL 2025

DOCUMENT APPROVAL

VERSION NUMBER	DATE	CREATED BY	APPROVED BY	SIGNATURE OF APPROVAL
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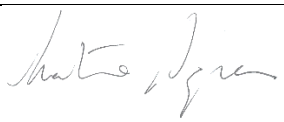
			Marline Squance	

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2 INTRODUCTION

Key elements of Data Management Plan (DMP) include database design, data entry, data checking and cleaning, site monitoring, appropriate maintenance of blinding of allocations to interventions and outcomes, data access, operational reports, reporting of interim and final analyses, dataset locking, database locking, and archiving. As an adaptive platform trial, most of these elements will be occurring throughout the lifetime of the trial.

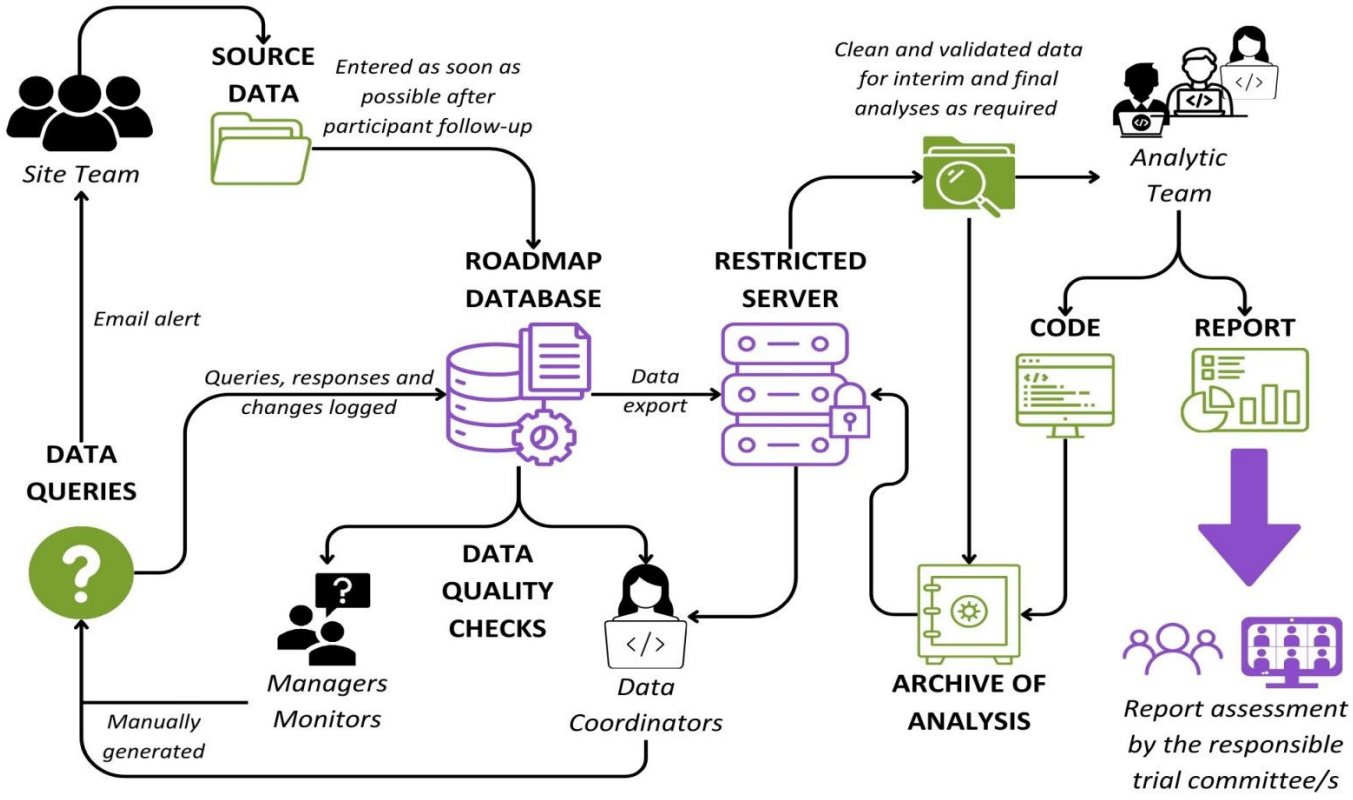

Figure 1 Overview of the processes in the data management for the ROADMAP Trial

2.1 PURPOSE

The purpose of this document is to provide detailed data management procedures and related responsibilities for the RandOmised Arthroplasty infection worlDwide Multidomain Adaptive Platform trial (ROADMAP).

2.2 UPDATE & REVIEW

This document will be updated throughout the life of the trial to reflect any changes in data management procedures. It should not be used in isolation. This DMP will be updated when and if new domains are added to the trial.

The DMP will be reviewed periodically when changes to data management working practices occur, for example following a substantial protocol amendment. When a new version is created, it will be reviewed and approved by those listed on the cover page, and a reason for revision will be listed in the revision history table.

The review process will:

- Address issues identified in the DMP and any other quality documents
- Document any new risks identified during the trial and inform updates to other relevant quality documents (where applicable)
- Ensure compliance with the ROADMAP trial protocols, appendices, and Standard Operating Procedures (SOPs)

2.3 TRIAL SUMMARY

ROADMAP is an investigator-initiated, randomised, embedded, multifactorial, adaptive, platform trial, conducted across multiple hospitals globally. Eligible, consenting participants will be randomly allocated to a prescribed regimen of interventions selected from multiple treatment domains. The platform enables the introduction of new treatments and/or domains as the trial progresses. See the core protocol and protocol appendices for details, available at www.roadmaptrial.com

2.4 TRIAL OBJECTIVES

The objective of ROADMAP is to identify the effect of a range of clinical interventions in participants with prosthetic joint infection (PJI) up to 12 months after platform entry. The ROADMAP platform aims to collect treatment and outcome data accurately and efficiently to evaluate the comparative effectiveness of alternative treatments. The platform is designed to be flexible and can accommodate additional interventions, either within existing domains or as part of new domains.

The secondary objectives of the ROADMAP trial include:

1. To examine the effect of a range of interventions on several secondary endpoints including mortality, patient-reported outcome measures, and healthcare costs.

2. To establish a biospecimen repository of PJI isolates linked to clinical outcomes to elucidate the pathogen-specific characteristics that underlie responses to different therapies.

3. To establish an observational registry of patients presenting with PJI but who are ineligible for or do not provide consent for the randomised platform.

3 GLOSSARY

A glossary of abbreviations and a glossary of database user profiles has been included for clarity.

3.1 GLOSSARY OF ABBREVIATIONS

Term	Definition
AES	Advanced Encryption Standards
AT	Analytic Team
AWS	Amazon Web Service
CON	Consent
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
CRQ	Change Request Quote
CSV	Comma Separated Values
Confidential Information	
DAIR	Debridement, Antibiotics and Implant Retention
DCO	Data Coordinator unblinded
DDesc	Data Description
DDict	Data Dictionary
DMP	Data Management Plan
DSA	Domain Specific Appendix
DSMC	Data and Safety Monitoring Committee
DSWG	Domain-Specific Working Group
DUAF	Database User Activation Form
eCRF(s)	Electronic Case Report Form(s)
EDC	Electronic Data Capture

Term	Definition
EL	Eligibility
FOI	Focus of Infection
GDPR	General Data Protection Regulation
GTMG	Global Trial Management Group
GTSC	Global Trial Steering Committee
Identifiable Data	Data collected of a personal and individual nature which can be used to identify the individual.
MedDRA	Medical safety data review and coding of safety events
NZDT	New Zealand Daylight Saving Time
NZST	New Zealand Saving Time
PD	Protocol Deviation
Personal Data	Any information relating to an identified or identifiable natural person ('data subject'); an identifiable natural person is one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person.
Platform	Patients in the platform are those who meet all core eligibility criteria and consent to inclusion in the platform. Occasional patients in the platform will not receive any randomised intervention (if they are not eligible for any available domain).
Platform entry	"Platform entry" is the timepoint when the patient has met core eligibility criteria, given informed consent for the platform, and been randomised
PJI	Prosthetic Joint Infection
RAR	Response Adaptive Randomisation
Registry	Patients in the registry include all those in the platform (as defined above) PLUS the "registry only" patients. Registry-only patients are those who are not in the platform, but who have consented to being in the registry.
ROADMAP	RandOmised Arthroplasty infection worldwide Multidomain Adaptive Platform trial
RTMG	Regional Trial Management Group
RTSC	Regional Trial Steering Committee
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAR	Serious Adverse Reaction
SDV	Source Data Verification
SMP	Safety Management Plan
SOP	Standard Operating Procedure
SoW	Statement of Work
Stats-WG	Statistics Working Group
ToR	Terms of Reference
TMF	Trial Master File
TMG	Trial Management Group
UAT	User Acceptance Testing
UST	Unblinded Statistician
UTC	Universal Time Zone
VPC	Virtual Private Cloud
WG(s)	Working Group(s)
Wireframe	Wireframe refers to the private online specification method Spiral uses to define a project. Very similar to a mock-up.
WD	Withdrawal

3.2 GLOSSARY OF DATABASE PROFILES

User Group	Breadth of Access	Details of Access
Co-ordinating Chief Investigator(s) (CCIs)	Global	Access includes: • Access to the user list including invitations and revocations • Update and modify help text • Report downloads available for global and/or region-level patient enrolment (including domain participation) and data completeness • On-screen global and regional recruitment figures for platform and registry
Regional Lead Investigator(s) (RLIs)	Regional	Access includes: • Report downloads available for region-level patient enrolment (including domain participation) and data completeness • On-screen global and regional recruitment figures for platform and registry
Site Principal Investigator (SPI)	Local	*Principal investigator/lead investigator at the site.* Access includes: • Patient screening and randomisation • CRF data entry • Sign off on Protocol Deviations • Report downloads available for site-level patient enrolment (including domain participation) and data completeness • On-screen global and site recruitment figures for platform and registry
Site Associate Investigator (AIV)	Local	*Associate investigator/sub investigator /co-investigator at the site.* Access includes: • Patient screening and randomisation • CRF data entry • Report downloads available for site-level patient enrolment (including domain participation) and data completeness • On-screen global and site recruitment figures for platform and registry
Research Coordinator (RSC)	Local	*Research coordinators/research nurses/study coordinators/other support staff at the site.* Access includes: • Patient screening and randomisation • CRF data entry • Report downloads available for site-level patient enrolment (including domain participation), data completeness • On-screen global and site recruitment figures for platform and registry
Regional Manager (RMG)	Regional	*Regional trial managers, trial coordinators, project managers* Access includes: • Read only view of all participant data at each site in region • Monitoring view of all participant data at each site in region for raising queries • Report downloads available for patient enrolment (including domain participation), data completeness, patient alerts, consent withdrawals, index isolates, users and location statuses in that region • Monitoring Tab and database queries • Upload region-specific resources • On-screen global recruitment figures for platform and registry • Location settings access for site set-up and modification • Access to the user list including invitations and revocations
Regional Data Coordinator (RDC)	Regional	*Regional data coordinators and data managers* Access includes: • Read only view of all participant data at each site in region • Monitoring view of all participant data at each site in region for raising queries • Report downloads available for patient enrolment (including domain participation), data completeness, patient alerts, consent withdrawals, users and location statuses in that region • Monitoring Tab and database queries

		• Upload region-specific resources • On-screen global recruitment figures for platform and registry • Location settings access for site set-up and modification • Access to the user list including invitations and revocations
Regional Monitor (RMO)	Regional	*Regional monitors/auditors* Access includes: • Read only view of all participant data at each site in region • Monitoring view of all participant data at each site in region for raising queries • Report downloads available for patient enrolment (including domain participation), data completeness, patient alerts, consent withdrawals, users and location statuses in that region • Monitoring Tab and database queries • Upload region-specific resources • On-screen global recruitment figures for platform and registry
Data Coordinator – unblinded (DCU)	Global	*Central data coordinator(s) only (unblinded)* Access includes: • Read only view of all participant data • Monitoring view of all participant data • Report downloads available for patient enrolment (including domain participation), data completeness, patient alerts, consent withdrawals, users and location statuses for all regions • Read only view of Monitoring Tab and database queries • Upload all region-specific resources • On-screen global recruitment figures for platform and registry • Access to downloadable csv file exports of all CRFs, (including those containing primary endpoint data and randomisation allocations)
Data Coordinator – blinded (DCB)	Global	*Central data coordinator(s) only (blinded)* Access includes: • Edit access to all participant data (to assist with data corrections, deletions, and overrides) • Monitoring view of all participant data • Report downloads available for patient enrolment (including domain participation), data completeness, patient alerts, consent withdrawals, users and location statuses for all regions • Monitoring Tab access and database queries • Upload all region-specific resources • On-screen global recruitment figures for platform and registry • Location settings access for site set-up and modification • Access to the user list including invitations and revocations • Access to downloadable csv file exports of all CRFs (excluding primary endpoint data and intervention allocation data) • Update and modify help text
Trial Manager (TMG)	Global	*1x account for central trial manager only* Access includes: • Read only view of all participant data • Monitoring view of all participant data • Report downloads available for patient enrolment (including domain participation), data completeness, patient alerts, consent withdrawals, users and location statuses for all regions • Monitoring Tab access and database queries • Upload all region-specific resources • On-screen global recruitment figures for platform and registry • Location settings access for site set-up and modification • Access to the user list including invitations and revocations • Access to downloadable csv file exports of all CRFs, (including those containing primary endpoint data and randomisation allocations) • Update and modify help text
Project Manager (PMG)	Global	*Account for central trial managers only* Access includes: • CRF data entry (but cannot randomise patients)

		• Monitoring view of all participant data • Report downloads available for patient enrolment (including domain participation), data completeness, patient alerts, consent withdrawals, users and location statuses for all regions • Monitoring Tab access and database queries • Upload all region-specific resources • On-screen global recruitment figures for platform and registry • Location settings access for site set-up and modification • Access to downloadable csv file exports of all CRFs (excluding primary endpoint data and intervention allocation data) • Update and modify help text
Unblinded Statistician (UST)	Global	*Account for analytic team only* Access includes: • Report downloads available for patient enrolment (including domain participation), data completeness, patient alerts, consent withdrawals, users and location statuses for all regions) • Access to downloadable csv file exports of all CRFs (excluding primary endpoint data and intervention allocation data) • On-screen global recruitment figures for platform and registry
Emails Only Account (EMO)	Regional	*Account for Regional Management Teams to receive emails to a central inbox* • Email notifications only • No on-screen access

4 DATA MANAGEMENT RESPONSIBILITIES

The specific responsibilities of each party are outlined in each corresponding agreement, Terms of Reference (ToR) or Statement of Work (SoW) document.

Table 1, overleaf, provides a summary of all parties' responsibilities with regards to data management.

4.1 DATABASE PROVIDER (SPIRAL SOFTWARE)

The specific responsibilities of the database provider are outlined in the service agreement and Statement of Work (SoW).

4.2 TRIAL MANAGEMENT GROUPS (TMGs)

The specific responsibilities of the Global and Regional Trial Management Groups (GTMGs & RTMGs) are outlined in detail in the TMG Terms of Reference and in each corresponding sponsor agreement.

4.3 COMMITTEE & WORKING GROUP RESPONSIBILITIES

The specific responsibilities of the Global Trial Steering Committee (GTSC), Data Safety Monitoring Committee (DSMC),

Statistics Working Group (Stats-WG), Analytic Team (AT), and other working groups (WGs) are outlined in detail in the committee or working group's Terms of Reference (ToR).

4.4 SITE RESPONSIBILITIES

The specific responsibilities of each site are outlined in detail in the site agreements and investigator agreements.

Table 1 Summary of Data Management Responsibilities

Key:

- **R:** Primary Responsibility
  # = while RTMGs have access to update these settings; all changes should be undertaken by the GTMG unless urgent update required
- **S:** Support or Feedback responsibility
- **A:** Approval responsibility

  *= Data Management Plan only

  ^ = a qualified and designated safety reviewer will be delegated to review, confirm and add MEDdra code

Category	Data Management Responsibilities	Database Provider (Spiral)	Global Trial Management Group (GTMG)	Regional Trial Management Group (RTMG)	Global Trial Steering Committee (GTSC)	Data Safety Monitoring Committee (DSMC)	Other Working Groups (WGs)	Sites	Statistics Working Group (Stats-WG)	Analytic Team (AT)
Documentation	Trial Integrity documentation creation and updates		R	S						
	Maintain delegation of responsibilities log and send copies to regional sponsors at regular intervals			S				R		
	CRF guidance document(s) creation and updates		R	S						
Access	Data extraction from the trial database	S	R							R
	Management of user account and site settings in Spinnaker	S	S	R						
	Management of the share drives containing raw trial data and access approval		A R							R
Database	Database randomisation algorithm	R	R						R	R
	Database: design of CRF, settings, content, user interface	R	R	S			S A			
	Approve content of CRFs on the Spiral wireframe and data description		R A	S						

Category	Data Management Responsibilities	Database Provider (Spiral)	Global Trial Management Group (GTMG)	Regional Trial Management Group (RTMG)	Global Trial Steering Committee (GTSC)	Data Safety Monitoring Committee (DSMC)	Other Working Groups (WGs)	Sites	Statistics Working Group (Stats-WG)	Analytic Team (AT)
	Build, validate, and test the database before releasing update/s to the database	R	R A	S						
	Updating the live database and maintaining data integrity through the trial life cycle	R	R							
	Manage database change process (e.g. new reports, corrections) during the life of the trial	R	R	S						
	Site Set-Up and Location Settings Management	S	R	R						
	Data management support to sites and monitors	S	R	R						
Records	Timely completion and return of CRFs/data			R				R		
	Enrolment of participants and data entry			S				R		
	Data query generation		S	R						
	On-site monitoring (both preparing for and conducting site visits)		S	R				R		
	Patient record deletion	S	R A	R						
Validations	Monitoring		S	R				S		
	Timely data query resolution		S	R				R		
	Data chase, consistency checks, and cleaning		R	R				S		
	Data correction, editable fields			S				R		
	Data correction, fields that are locked	S	R	A				S		
Locking	Locking CRFs (independent of participant lock)		S	R						
	Locking participants (also locks all CRFs)		S	R						

Category	Data Management Responsibilities	Database Provider (Spiral)	Global Trial Management Group (GTMG)	Regional Trial Management Group (RTMG)	Global Trial Steering Committee (GTSC)	Data Safety Monitoring Committee (DSMC)	Other Working Groups (WGs)	Sites	Statistics Working Group (Stats-WG)	Analytic Team (AT)
	Locking sites		R	A						
Analysis	Data transfer to analysts	S	R						S	S
	ROADMAP Trial Platform and Domains: Data analysis, preparation, and circulation of the DSMC report		S							R
	Data review, recommendations and circulation of the DSMC letter of recommendations		S			R				S
	Responding to DSMC queries and recommendations		R		S A					R
	ROADMAP Trial Sub-studies: Data analysis, preparation, and circulation of the report		S				R		S	S
Support	Spinnaker database access request			R						
	Database Support request	R	S	S						

KEY:

- **R:** Primary Responsibility
- **S:** Support or Feedback responsibility
- **A:** Approval responsibility

^ = a qualified and designated safety reviewer will be delegated to review, confirm and add MedDRA code

5 DATA MANAGEMENT ACTIVITIES

The tables below shows specific data management activities in the ROADMAP trial, the primary and personnel responsible for each and, where applicable, a timeline for each.

Data management activities that relate to monitoring or safety monitoring will be detailed in the respective monitoring and safety management plans.

Table 2 Timescale of Data Management Activities

Category & Detail	Primary Responsibility (R)	Timescale
Documentation		
Review of the Trial Integrity Documentation	GTMG	Annually at a minimum
Review and update of the delegation of responsibilities log	Sites	Ad hoc as required
Review of the ROADMAP Spinnaker Video Guide	GTMG	Annually at a minimum
Access		
Data Extraction from the database	AT & GTMG (unblinded central data coordinator/s)	Every 500 participants
Management of User account and site settings in Spinnaker	RTMG & GTMG	Ad hoc as required
Access to the University of Newcastle Research Data Share Drive	GTMG (unblinded central data coordinator/s)	Within 2 weeks of the request *A response will be received by the applicant within 2 weeks of a written request to the Research Computing Activity Owner, provided all required documentation for the user is present*
Database		
Database randomisation algorithm	Database provider, GTMG, Stats-WG, AT	Ongoing *As required (e.g. changes to the database to reflect protocol updates)*
Database: design of CRF, settings, content, user interface	Database provider, GTMG, Other WGs	Ad hoc as required
Approve content of CRFs on the Spiral wireframe and data description	GTMG	Ad hoc as required
Build, validate, and test the database before releasing update/s to the database	Database provider & GTMG	Ad hoc as required
Updating the live database and maintaining data integrity through the trial life cycle	Database provider & GTMG	Ongoing *As required (e.g. changes to the database to reflect protocol updates)*
Manage database change process (e.g. new reports, corrections) during the life of the trial	Database provider & GTMG	Ongoing *As required (e.g. changes to the database to reflect protocol updates)*
Site Set-Up and Location Settings Management	GTMG & RTMGs	Ongoing *As required (e.g. changes to site participation, permissions & protocol updates)* ***Note:** while RTMGs have access to update these settings; all changes should be undertaken by the GTMG unless urgent update required
Data management support to sites and monitors	GTMG & RTMGs	Ongoing
Records		

Timely completion and return of CRFs/data	Site	Ongoing
Completion of the Day 100 follow up CRF		By Day 110 (within 10 days of completion due date)
Completion of the remainder of the Day 365 follow up CRF		By Day 365 + 30 days (within 30 days of completion due date) *eCRF completion timelines are specified in the core protocol and the ROADMAP Spinnaker Video Guide.*
Enrolment of participants	Site	Ongoing
On-site monitoring (both preparing for and conducting site visits)	Site & RTMG	As per Monitoring Plan *Monitors to conduct on-site monitoring visits as per their region-specific monitoring plan.*
Patient record deletion	GTMG	Within 2 days of request *A record deletion request will be actioned within 2 working days of a written request by the RTMG.*
Medical safety data review and MedDRA coding of safety events	RTMG	As per Safety Management Plan *The MedDRA coding is required to be added as per timelines outlined in region-specific safety management documentation.*
Validations		
Data query generation	RTMG	Ongoing *RTMGs to raise queries within the database system, as required, and upon receipt of a data completion report.*
Timely data query resolution	Site	Within 7 days of the query being raised
Data Cleaning		Ongoing
Data cleaning and consistency checks for the Priority Datapoints	GTMG & RTMG	Within 14 days of each 500th participant reaching day 365 *Data cleaning will be performed on the block of 500 participants that will be included in the interim analysis. These cleaning and consistency checks will be performed for the key variables that will be reviewed as part of this analysis. Data cleaning will be a continuous process led by the GTMG and the RTMGs. RMTGs remain responsible for the data in their region.*
Data cleaning and consistency checks for 'Other' fields		Monthly, for all participants enrolled *Data cleaning will be a continuous process led by the GTMG and the RTMGs. RMTGs remain responsible for the data in their region.*
Final data clean		Prior to a final analysis/manuscript *A detailed data clean will be performed when a final analysis for results publication is required.*
Data Corrections		Ongoing
Data corrections, editable fields	Site	Within 7 days of the query being raised
Data corrections, non-editable fields for Priority Datapoints	GTMG	Within 7 days of request *A data correction request will be actioned within 7 working days for key variables & fields that can be corrected by the GTMG*
Data corrections, non-editable fields for 'Other' fields	Database provider	Prior to final analyses *For fields that require Spiral Software to perform the correction. Fields that cannot be corrected by the GTMG will be logged centrally for correction prior to the final analyses*
Locking		
Locking CRFs (independent of participant lock)	RTMGs	Ongoing
eCRF locking, Day 365 CRF	Database provider	By day 365 (Baseline and Day 100) and by day 395 (Day 365)

		CRF auto-locks at the above timepoints to prevent modification of the primary endpoint data.
eCRF locking, all other CRFs	RTMGs	Prior to a final analysis/manuscript *CRFs will remain unlocked until final data cleaning has occurred for a result publication.*
Locking participants (also locks all CRFs)	RTMGs	Prior to the final analysis/manuscript *Participant CRFs will remain unlocked until final data cleaning has occurred for a result publication.*
Locking sites	GTMGs	Upon site closure *Sites will be locked, and access removed at the point that the site has been closed to recruitment and there are no outstanding data queries.*
Analysis		
Data transfer to analysts	GTMG (unblinded central data coordinator(s))	Within 2 weeks of the trigger for analysis being reached *Within 2 weeks of each 500th participant in the platform having reached day 365*
Generation of the Open and Closed DSMC Reports (analysis, preparation, and circulation)	AT	Within 3 weeks of the data transfer
Report reviewed and confirmed	GTMG	Within 1 week of report generation
Data review and DSMC meeting	DSMC	Within 2 weeks of report confirmation
DSMC letter of recommendations	DSMC	Within 1 week of DSMC meeting
Responding to DSMC queries and recommendations	GTMG & GTSC	Within 1 month of receipt of queries and recommendations
ROADMAP Trial Sub-studies: Data analysis, preparation, and circulation of the report	Other WGs & AT	Ad hoc as required *The AT and DSMC will not be responsible for analysis, review and recommendation of the sub-studies unless negotiated.*
Support		
Spinnaker database access request	RTMG	Within 2 working days of the request *Access to the Spinnaker database will be provided within 2 days of the request, provided all required documentation for the user is present*
Database Support request	Database provider, GTMG & RTMGs	Within 2 days of the request *A response to a database support request (submitted via the feedback button on the database, or via email) will be returned as soon as possible and within 2 working days.*

6 DATABASE DESIGN

The Spinnaker database was developed in conjunction with, and is hosted by the Database provider, Spiral Software Ltd (Spiral), New Zealand. Spiral will provide and maintain the software platform (Spinnaker) during the trial.

The Spinnaker database is presented in English and is compatible with standard web browsers, tablets, and smartphones and comprises of the trial database platform, database eCRFs, audit log and data exports and reports.

- The trial database platform is the database itself, which includes the site and location settings, user profiles, domains and interventions, resources, and management modules.
- The database eCRFs are accompanied by an online data description (DDesc) spreadsheet that is jointly managed by Spiral and the GTMG. The DDesc outlines all questions within the eCRFs and provides a description of the rules governing the questions (logic), including show/hide rules for specific participants, acceptable value ranges, etc.
- Database reports, including operational reports, will be available as viewable reports within the Spinnaker database and/or as downloadable exports (Excel files in .csv format).

- All raw data exports and database reports will have a conventional label, and a timestamp reflecting the date and time in which the export was downloaded.

6.1 DATA PROTECTION, SECURITY & COMPUTATIONAL ARCHITECTURE

Data are stored in Australia. Australia has a data protection law, and an independent data protection authority accredited at the international conference of data protection and privacy commissioners.

Spinnaker data are backed up to a server within the Amazon Web Service (AWS) zone and on S3 encrypted server according to the AWS Standard Security Protocol. Backups occur every hour and every 6 hours onsite and offsite respectively. AWS firewalls both internally and externally are in place for intrusion protection.

Spinnaker software platform ensures encryption of personal data using Advanced Encryption Standards (AES) for participant confidentiality and integrity. A data logging system is used to track user access to personal data included any changes, deletions, updates made by the user. For further information on data protection for the Spinnaker Platform and Spiral please contact Spiral at audrey@spiral.co.nz.

A summary table of security and computational access is provided below – for any further questions, please contact Audrey Shearer (Founder and CEO, Spiral):

- Email: audrey@spiral.co.nz

Table 3: Security and Computational Architecture

Name of operating system	Spinnaker Software Platform on Microsoft .NET IIS server running on Windows Server, made up of a Microsoft .Net application with a SQL Server back end.
Computer system	Constituted of one (1) or more externalised servers, externalised to AWS, Sydney Australia.
Application software implements	A database namely Microsoft SQL Server
Nature of the organisations computer network used for process	Communications with the outside world i.e. The internet
Processing	Processing involves exchanges with users, a host and external third parties (organisations, partners, clients, etc). These internet exchanges include: • Web portal • File transfer • Email
Methods for transfer of digital material	All internet traffic via HTTPS TLS1.2
Physical security of premises and equipment	AWS Standard Security Protocols see AWS Sydney Zone Protocols available online
Backups	Backups are to another server within the AWS Zone and on S3 encrypted storage. • Onsite backups occur every hour • Offsite backups occur every 6 hours AWS Standard security features secure the physical media
Intrusion Protection	End Point Protection (Antivirus) is installed on all servers involved in the hosting of the Spinnaker Database. Two (2) Firewalls are in place: • The AWS Firewall

	• An external Firewall provided by Cloudflare The platform is isolated from other platforms (e.g. VLAN) The platform is restricted to processing within its own virtual private cloud (VPC)
Data confidentiality during development of the computer application	Development and production environments are distinct Development is based on a combination of fictitious and anonymised data
Data confidentiality during software or equipment maintenance operations	Software is subject to remote maintenance Risks are mitigated as per ISO27001 procedures Security clearance for accessing personal data files, on the rare occasion, when necessary, is restricted to one person on the software maintenance team
Authentication/identification of persons entitled to access the application	Authorization profiles define the functions or types of information accessible to a user Logical access control is carried out with a password which is one way encrypted with SCrypt
Data logging to application	Data logged includes: • Date/time of connection • IP Logging • User identifier • Date/time of lockout/tagout • Operation performed • Failed login attempts • Error logging
Data logging of access to personal data	Data logged includes: • Date/time of connection • User identifier • Creation changes • Update changes • Deletion changes
Confidentiality/integrity processes	• Encryption of stored personal data using the AES Rijdael • Key length = 256 bit • Security protocol used is TLS1.2 and 1.3 • Server authentication uses TLS 1.3, X25519, and AES_256_GCM • Server authentication issued by Trustico RSA DV A

6.2 RANDOMISATION STRATEGY

Randomisation is performed within the ROADMAP trial database (Spinnaker) by a randomisation engine integrated into the eligibility module for screening and enrolling participants. Randomisation engines (random number generators) typically need a seed value, often time based. The database provider will "double seed" the generator with a combination of time and unique eligibility ID to create a "very random" selection.

At first, simple randomisation will be instated, meaning that randomisation ratios will be balanced (1:1 ratio). Throughout the lifecycle of the trial, it may be decided to implement Response Adaptive Randomisation (RAR). If this decision is made, the randomisation engine will randomise patients based on a set of regimen codes with associated ratios supplied by the AT.

Most domains will use a simple randomisation algorithm, meaning that the ratio will be spread across all regions. This could lead to local randomisation imbalance within a country, however, due to the projected large number of participants recruited to the trial, it is expected that this imbalance will be negligible. For smaller domains, block randomisation stratified by country or by site, may be used to ensure there is appropriate balance.

6.2.1 RANDOMISATION OVERVIEW

Upon confirmation of participant eligibility to the trial and consent to the domains, treatment allocations will be generated for each participant; any allocations that are not possible (site is not participating in a domain or the participant did not consent) will not be generated for the participant.

Randomisation allocations will then be generated for all domains that the participant has the opportunity to be assessed for:

- **Participant is eligible** = allocation revealed
- **Participant is not eligible** (due to meeting exclusion criteria and/or not being assessed within the required timeframe) = allocation is not revealed

Allocation reveal is a staggered process, as there are different timepoints associated with eligibility assessments. At the end of the eligibility timepoints, the participant could have up to three randomisation allocations.

6.2.2 VALIDATION OF THE RANDOMISATION ALGORITHM

The randomisation algorithm is validated by the database provider by randomising with the same participant settings using scripts. The same validation check is also conducted by the blinded statisticians from the Stats-WG.

Validation of the randomisation algorithm will be conducted each time a domain is opened, or annually, at a minimum. Additional ad hoc validations can occur as requested by the GTSC or Stats-WG.

The randomisation algorithm will be validated by the database provider and Statistics WG at the following timepoints:

- Beginning of the trial (March 2025)
- Upon Reaching 100 participants
- Upon Reaching 1000 participants
- Opening of new domain/s (TBD)

6.3 DATABASE BUILD & MANAGEMENT

The build and management of the database and liaising with the database provider will be the responsibility of the GTMG, who will work closely with the database provider.

The database will be developed and managed using the following tools, as specified by the database provider (Spiral):

6.3.1 DATA DESCRIPTION (ONLINE GOOGLE DOC)

This document is used to for the initial development of the database CRFs and to manage and record any changes that are required to the CRFs once built.

This is a working document that shows the current state of the CRFs, including the details and order of the question text and subtext, as well as providing details regarding the logic and limitations of each question.

The database provider has ownership of this document and edit privileges are delegated to the GTMG for certain fields.

6.3.2 DATA DICTIONARY (SPINNAKER DATABASE EXPORT)

This export is a direct download of the database that is used to provide context to the data exports for the analytic team (AT) who is conducting the interim and final analyses. Like the Data Description (DDesc), the Data Dictionary (DDict) shows the current state of the CRFs, including the details of the question text and subtext, as well as providing details regarding the logic and limitations of each question.

6.3.3 WIREFRAME (PROOF-OF-CONCEPT TOOL)

The Wireframe is a two-dimensional illustration of the database that specifically focuses on the prioritisation of content, functionalities available, and intended behaviours.

The Wireframe represents the finished user interface but may exclude styling, colour, and graphics; it assists in establishing relationships between the CRF's various elements, the CRF as a whole, and the database.

6.3.4 STAGING ENVIRONMENT (TEST DATABASE)

The staging environment is an exact replica of a production environment that is used for testing the database functionality. The staging environment provides a functioning database to test changes made, to ensure quality under a production-like environment before real world deployment.

The staging environment also provides a functioning database to test the current database behaviour when issues and bugs are discovered.

6.3.5 USERBACK (ONLINE TICKET PORTAL)

The Userback portal is used to communicate all changes requested to the database; Userback tickets can be logged by any database user via the feedback button on the database.

These tickets are reviewed and organised by the GTMG in collaboration with the database provider and will be used to identify the changes requested on the reports.

6.4 DATABASE REVIEW & APPROVAL

Review of the database is an ongoing process that will be overseen by the GTMG, including the Co-ordinating Chief Investigators of the trial, in collaboration with the database provider.

The database as a whole will be reviewed any time a change to the trial is made. If any changes are required, the procedures outlined in **Section 8** will be followed. When changes are made to the database, the updates will be reviewed and approved by the GTMG. If relevant, the RTMG, WGs and others may be involved in the review and approval. All changes to the database will be communicated to RTMGs and to all study sites (via RTMGs).

A comprehensive record of all changes to the database will be maintained by the GTMG.

7 CASE REPORT FORM (CRF) DESIGN

The ROADMAP Trial will use eCRFs to complete data entry. It is expected that the eCRFs are completed in real-time.

- Sites may use paper forms (such as the EQ-5D paper form or the screening and enrolment log) to collect data; these are tools only and are not considered source data. It is expected that this information is all entered into the database as soon as possible.
- Most regions will obtain patient consent on paper consent forms, with a wet-ink signature. These are considered source data and should be stored in accordance with, and for the duration specified by regional regulations.

7.1 CRF FORMATTING STYLE

The eCRFs within the Spinnaker database comprise of the following:

- CRF name
- Heading/Section Name (sometimes including a heading/section number)
- Question Text (sometimes including a question number)
- Subtext
- Answer field (yes/no buttons, free text fields, tick boxes, date and time fields, value entry fields, toggle table fields)
- Help Text (available by clicking into the question mark button next to each question)

The eCRFs within the Spinnaker database are embedded with the following logic:

- Built in alerts (including protocol deviation, missing field, safety event reminders that appear based on the data that is entered)
- Built in amber and red ranges (to alert sites to values that are not expected, to avoid data entry mistakes)
- Integrated email reminders (optional email alerts can be received to ensure that no important events/timepoints are missed)

Please see the ROADMAP Spinnaker Video Guide for more information.

7.2 CRF REVIEW & APPROVAL

All versions of all trial CRFs are reviewed and approved by the GTMG, including the Co-ordinating Chief Investigators of the trial.

The CRFs will be reviewed any time a change to the trial protocols is made, to ensure alignment with the updated protocols. If any changes are required, the procedures outlined in **Section 8** will be followed.

A comprehensive record of all changes to the database is maintained by the GTMG.

7.3 TRIAL CRFs

The table below shows all core CRFs for the trial and a form date for each (i.e. the field on the CRF that is considered the form date).

Vital status is collected on Day 100 and Day 365 CRFs for platform participants, and Day 365 CRFs for registry-only participants. Exact date of death, or if unknown, last known date alive is recorded. Last known date alive can be infered from records of clinic visits; blood or radiology tests; doctors letters; or any other indirect evidence that the patient was alive on a given date.

All CRFs are expected to be completed by designated site staff (Principal Investigators, Associate Investigators, Research Nurses/Coordinators). All source data is expected to be collected at trial sites.

7.3.1 PLATFORM CRFs

Each domain may have additional domain-specific CRFs that will be required for completion; these will be specified in theROADMAP Spinnaker Video Guide . Completion timelines are further clarified in the core protocol.

- Platform Eligibility, Consent, Withdrawal and Consent (Regained Capacity) CRFs contain dates of data completion. These appear in the form of 'Date of Screening'; 'Consent obtained at'; 'Date of Withdrawal'; and 'Consent obtained at', respectively.

7.3.2 REGISTRY CRFS

Completion timelines are further clarified in the registry appendix.

- Platform Eligibility, Consent, Withdrawal (Registry) and Consent (Regained Capacity) CRFs contain dates of data completion. These appear in the form of 'Date of Screening'; 'Consent obtained at'; 'Date of Withdrawal'; and 'Consent obtained at', respectively.

7.4 HELP TEXT

The help text can be accessed by clicking the information button next to question text in the database. Help text is used to add further clarifications to the questions, including examples, region-specific nuances and guidance, and detailed definitions. Please note that help text can be updated at any time by the GTMG, without the assistance of the database provider (Spiral). This makes it a very useful resource to use for communicating and clarifying questions with the sites.

In most situations, the help text will be updated to provide clarifying information regarding the phrasing of a question and/or to provide useful examples as references. Therefore, the question text and subtext will only be updated when it is incorrect or globally misunderstood.

7.5 CHANGE LOG

The change log provides a record of all updates made to participant CRFs, including a summary of initial data entry and subsequent changes for all database fields for that participant. A change log is available for each participant in the database, to track all changes to the data and CRFs made by any user.

This change log is a readable, user friendly, 'front end' version of the 'back end' audit log. This audit log is used to track all activity in the database and is kept on New Zealand servers. As such, the audit log is tracked in NZ standard time (NZST; UTC-12), as it is reading this audit log as it source.

8 MAKING CHANGES TO THE DATABASE

Changes will be made to the trial database as appropriate, including but not limited to the following situations:

- New aspects of the trial are introduced (such as a new domain or protocol update)
- In response to bugs/faults discovered in the database behaviour
- It is agreed that a feature of the database is not fit for purpose
- A change is required for the purposes of the analyses

All requests for changes must go through the GTMG who will liaise with the database team (Spiral) to make these changes. The GTMG will organise requested changes into database releases (known as 'sprints'), where changes will be grouped based on 1) priority/urgency and 2) relevance to one another.

For example, a sprint may include all changes relating to the Day 100 CRF.
For example, a sprint may include all changes that have been urgently requested across multiple regions

For each change, a decision will be made regarding its scope:

- New participants only: Changes will apply only to participants enrolled after the update is implemented.
- Subset of participants: Changes may apply to specific groups (e.g., certain domains, paediatric participants, participants from a particular region).
- Protocol version-specific: Changes may apply only to participants enrolled under a specific protocol version (e.g., protocol version 2.0).
- All participants: Changes will apply to the entire database, affecting all completed CRFs and follow-up data.

Changes, in general, can and will be implemented without any downtime to the database. When a change has been released to the live database site, the GTMG will notify all relevant persons including the RTMGs, site staff and working groups as required. The -ROADMAP Spinnaker Video Guide will be updated as applicable.

Table 4 Example Changes to the Database or CRFs

Changes to the CRFs
May include: • Addition of new CRFs, question text or subtext • Addition/change to database alerts, email notifications, and on-screen reminders • Addition/change to allowable values (amber and red ranges) • Change to question text or subtext
Other Changes to the Database
May include: • Addition/change to the reports or export • Addition/change to the user profiles or profile permissions

- Addition/change to the email notifications
- Addition/change to the available location settings (metadata)
- Other changes to database functionality

8.1 PROCESS FOR IMPLEMENTING CHANGES TO THE DATABASE

The process for implemented changes to the database or CRFs is as follows:

- The GTMG ensures all requested changes are logged in **Userback**; all requests must have a Userback ticket created
- The GTMG update the **DDesc** in collaboration with the database provider (Spiral)
- The database provider develops the changes within **the Wireframe**; the Wireframe is then reviewed by the GTMG (and any other relevant groups)
    - If any changes are requested, the database provider will update the Wireframe for re-review
    - The Wireframe will be approved by the GTMG
    - The Database provider will update the DDesc to match the approved Wireframe
- A **Change Request Quote (CRQ)** is issued by the database provider for review
    - If the CRQ is not accepted, the Wireframe/DDesc may go through an iterative process to come to an agreement before final acceptance or rejection.
    - The CRQ will be approved or rejected by the GTMG
    - A CRQ will not be required if the change is a bug fix
- Accepted changes will go through the coding process before release on the staging environment for **User Acceptance Testing (UAT).**
    - The GTMG will be responsible for UAT but may request assistance from RTMGs or other users to complete this process.
    - If there are issues noticed during UAT, feedback will be provided to the database provider via Userback and the changes re-released once issues are corrected.
    - UAT will be approved by the GTMG.

Once the above steps are complete, the changes are **released to the live database.**

8.2 DOCUMENTING CHANGES TO THE DATABASE

Documentation of database changes is maintained by the via the following methods:

- **Sprint Reports** –summarise all changes made as a result of a particular sprint (managed by database provider [Spiral])
- **Database Sprint Summary** – available within the database to select user profiles; provides a succint summary of sprint releases
- **Archived Userback Tickets** – provide a history of all requested changes to the database

All changes to the database will additionally be documented and tracked by the GTMG. The DDesc and DDict will reflect the current version of the database and will incorporate all released changes.

8.3 DISTRIBUTION AND INFORMATION OF DATABASE CHANGES

Database users will be informed via email of all changes to the database.

When a release is made, relevant changes will be added to the - ROADMAP Spinnaker Video Guide, and all sites provided with the updated version.

9 DATABASE USER ACCESS

Access to the database is restricted to users who have had a profile created within the Spinnaker database environment. The user account is password protected and must be linked to a unique email address.

A list of all active and historical database users is available as an export from both the live and staging environments.

9.1 ACCESS TO THE STAGING ENVIRONMENT

Any member of the ROADMAP community can request access to the staging environment. All access requests will be processed by the GTMG. Region-specific generic accounts will be created by the database provider (Spiral), and users will be provided with the login details.

9.2 ACCESS TO THE LIVE ENVIRONMENT

Access to the live environment is available to trial site staff and regional and global management staff.

To request access, each user must complete a Database User Activation Form (DUAF), and provide the required training, delegation and documentation to the RTMG, who will establish the user within the database.

The user will receive an email directly from the Spinnaker database instructing them to activate their account and create a unique password. If required once activated, the user can have access to one or more sites within the database.

The date that access is granted to the live environment will be recorded on the DUAF and available from the Location Status Export.

9.3 REVOKING OF ACCESS

Access to the live environment should be revoked once the user has ceased working on the ROADMAP Trial at a site/s or overall.

When a database user has ceased work on the ROADMAP trial, the RTMG will change their user profile status to 'locked out' and record the date of revocation on the DUAF. The user will no longer be able to access that site/s or the database as a whole.

The date that access is revoked to the live environment will be recorded on the DUAF and available from the Location Status Export.

10 PARTICIPANT MANAGEMENT

Participants should be managed according to the protocol, region-specific guidance documents, and the ROADMAP Spinnaker Video Guide.

Depending on site procedures, participant screening data may be required to be entered into an additional database (such as REDCap etc.).

10.1 PARTICIPANT IDENTIFICATION CODES

The participant is assigned two different codes: a participant screening ID when the participant has been screened, and an additional trial ID when the participant is enrolled into the trial (either platform or registry).

10.1.1 PARTICIPANT SCREENING ID

During platform screening, each participant is given a six-letter alphabetic ID. This identification number is used to identify each unique participant, prior to completion of platform eligibility and consent. If the participant is not eligible for the trial, or are eligible but consent is not completed (i.e., CRF is not completed), the Screening ID remains their assigned code. If the participant is enrolled into the platform or registry, they are assigned a Trial ID alongside their Screening ID. The Screening ID remains visible alongside the ROADMAP Trial ID when viewing platform screening data in Spinnaker or when viewing the eligibility data export.

10.1.2 PARTICIPANT TRIAL ID

After platform eligibility screening has been completed and the participant is randomised, a new 11-digit trial ID number is assigned.

The ROADMAP Trial ID comprises two letters designating the country code, followed by three letters designating the site code of the enrolling site, followed by a hyphen ("-"). The next five are allocated sequentially per site, in the order of enrolment into ROADMAP. Registry-only participants are intercalated within this sequence and are designated with the suffix "-R" after the site code. If a patient is removed from the database for whatever reason, their unique number will be archived and cannot be reused thus, a sequential list of participants at a site may be as follows:

- AUABC-00001
- AUABC-00002
- AUABC-00003-R
- AUABC-00005*

  ** AUABC00004-R is skipped as participant was removed from the database*

The site codes used are listed in the international site tracker and are assigned by the RTMGs. The RTMGs will be responsible for checking with the GTMG to ensure the site code has not already been used. All site codes are unique and reflect the name of the site in some manner.

10.2 PARTICIPANT TRACKING

Participants can be tracked in the database by using the participant list. This list provides an overview of each participant enrolled at the site; their randomised domains (including 'pending' or 'NE' [Not Eligible] where applicable); and a summary of the CRFs that are either completed, require completion, or are not required.

Please see the - ROADMAP Spinnaker Video Guide for more information about how to manage participants within the database.

10.3 INELIGIBILITY DISCOVERED AFTER ENROLMENT

If a participant is discovered to be **ineligible after enrolment** because they **have not met one or more of the core inclusion criteria** (e.g., did not have a knee or hip PJI) or, they have **met one or more core exclusion criteria**:

- **if randomisations have not been revealed**, the participant should be withdrawn from the trial
- **if any randomisations have been revealed,** the participant should remain within the trial for those domains; data continue to be collected; and allocated interventions continue as long as this is still clinically appropriate.

11 SITE METADATA

Each site within the database will have its own unique location settings (metadata) that can be adjusted to match region and local requirements.

This includes aspects such as:

- Age of patients (18+ years)
- Participant identifiable information to be collected (DOB/age/etc.)
- Consent options (written/verbal/surrogate/waivers/etc.)
- Active domains (Surgical/Antibiotic Choice/Antibiotic Duration/etc.)
- Interventions available within a domain (when more than two treatment arms are available)
- Active sub-studies
- Other nuances not already listed, e.g., region-specific questions

The GTMG & RTMG have access to update the site location settings, however, the primary responsibility for activating and updating sites remains with the GTMG. The RTMG have access to implement changes if urgent update is required and are

responsible for reviewing site location settings upon each change to ensure correctness. All metadata will be documented using the Green Light Activation Form and Protocol Update Forms by the RTMG, and these forms will be updated with each iteration of the site location settings. Both the RTMG and GTMG will provide signature on these documents, confirming that the changes have been made to the database.

Site location settings can be viewed and checked at any time using the Location Settings export available to all RTMGs and GTMGs.

12 DATA ENTRY

Data is entered directly into the Spinnaker database by approved database users.

Data entry is required on an ongoing basis, according to the data entry timelines outlined in the Core Protocol and appendices, and in the ROADMAP Spinnaker Video Guide. The CRFs are designed to be pragmatic – minimising the possibility of missing data and streamlining the validity of the entered data by prespecified validity checks.

12.1 MINIMISING MISSING DATA

The database will automatically grey out CRFs that are not applicable to the participant, based on answers provided in the database. Therefore, to ensure the database can implement this logic correctly, the CRFs should be completed in the order in which the events occur for that participant.

CRFs that are incomplete or not started will be denoted by an orange question mark or red cross, respectively; only CRFs that are entirely complete will achieve a green tick, denoting completion.

If all or part of a CRF cannot be completed, the site can request a data override to be completed.

12.2 STREAMLINING VALIDITY OF DATA ENTRY

Automatic validity and consistency checks are implemented within the database (e.g., range checks for datapoints, and consistency of dates) to assist sites in entering correct data. Warnings may appear when a data entry contradicts another field or what is reasonably expected for that field.

Additional data validation checks will be performed manually by the GTMG.

12.3 INTERRUPTIONS TO DATA ENTRY

If the usual data entry staff are out of office and not able to enter data as per the Core Protocol data entry timelines, the situation will be monitored by the RTMG, and a decision made regarding whether the site should pause recruitment until data entry issues can be resolved.

The GTMG and RTMG will be in communication with the site to ensure that the datapoints of highest priority are completed, and that any pauses to recruitment are logged and documented.

12.4 SIGN OFF OF DATA ENTRY

Some CRFs will require signature from specific user profiles in the database. A digital signature can be added to these CRFs to show that they have been reviewed and confirmed by the user; these types of sign offs are documented in the table below:

Table 5 Data Entry Requiring Sign Off

CRF Name	Sign off Required By	Reason	Database User Profile
Protocol Deviation CRF	Data Enterer	To document the user who entered the protocol deviation data	Research Coordinator (RSC) / Site Associate Investigator (SAI) / Site Principal Investigator (SPI)

	RTMG	To document RTMG review, confirmation and resolution of the event	Regional Manager (RMG)

Permissions for sign off will only be provided to specific user profiles to ensure that the sign off has been made by the authorised personnel.

13 DATA QUALITY CONTROL

The Spinnaker database has built in functionality to streamline the checking and completion for CRFs (See **Section 12 – Data Entry**). In addition to this embedded functionality, additional data completion and missingness, and data cleaning checks will be performed throughout the lifetime of the trial.

Due to the frequent scheduled analyses that occur for the trial, data quality control will be a continuous process. To assist with data quality control, the following summaries will be generated by the GTMG regularly for data quality oversight by the GTSC, RTSCs and RTMGs.

It remains the primary responsibility of each region to maintain their trial data and ensure accuracy and validity to the best of their ability.

Table 6 Data Quality Control Summaries

Summary Name	Detail	Type of Report	Timescale
Data Cleaning Summary	Summary of data inconsistencies and errors for correction	Regional	Every 4 weeks *Will be made available to the RTMGs via the Data Cleaning Report and can be shared with the RTSCs.*
Data Completion Summary	Summary of data completion and completion timeliness for CRFs by: • Site (regional only) • Region • Whole trial (global only)	Regional	Every 4 weeks *Will be made available to the RTMGs via the Data Cleaning Report and can be shared with the RTSCs.*
		Global	Every 4 weeks *Will be made available to the GTSC via the GTSC Report.*
Data Missingness Summary	Summary of data missingness for database fields by: • Site (regional only) • Region • Whole trial (global only)	Regional	Every 4 weeks *Will be made available to the RTMGs via the Data Cleaning Report and can be shared with the RTSCs.*
		Global	Every 4 weeks *Will be made available to the GTSC via the GTSC Report.*

13.1 DATA COMPLETION & MISSINGNESS

CRFs will only receive a green tick once all data fields have been completed. Each CRF will be checked to confirm that:

- The required datafields are complete
- If unable to be completed, that a data override will be performed centrally to document the field as unavailable
- That all alerts are resolved

A data completion report is accessible to all users within the database, so that each user can keep track of the site(s) they have access to, and the completion of their data.

Aggregated reports on data completion and timeliness of data completion will be provided by the GTMG to the GTSC and RTMGs as per **Table 9**. Line listing of relevant regional and site data completion will be provided to RTMGs.

13.2 DATA CLEANING

As per Section 12 (**Data Entry**) of this document, there are many embedded validities checks in the Spinnaker database that will encourage sites to enter correct and accurate data. In addition to these automatic validity checks, sites will undergo regular data cleaning and monitoring processes to ensure quality and integrity of the data. Details of the overall monitoring for the trial can be found in the Monitoring Plan; the aspects discussed here relate to data management only (data cleaning).

The GTMG will conduct regular and routine checks of the data to ensure consistency and quality of the data entered. The checks will be performed on priority datapoints to ensure the integrity of the scheduled interim analyses. Other checks will be run less frequently on the other datapoints within the database system by the GTMG and the RTMGs.

Monthly data cleaning reports will be communicated to the RTMGs, with a summary of any inconsistencies discovered with the priority datapoints and other datapoints based on a standard report template. Data exports will be checked with scripts developed by the GTMG to provide these aggregated reports at the whole of trial, regional and site levels. Line listing of relevant regional and site data inconsistencies will be provided to RMTGs via these data cleaning reports. Ad hoc checks will be communicated to the RTMGs on an ad hoc basis and can be incorporated into the report template as required.

The GTMG and RTMG can produce queries within the Spinnaker database against specific datapoints. It is expected that these queries are resolved within 7 days by the site, in communication with the RTMGs.

13.2.1 DATA CLEANING OF PRIORITY DATAPOINTS

Priority datapoints are ones which:

- Will affect the participant's enrolment into the domains and progression through the trial
- Are imperative for the conduct of the interim scheduled analyses
- Are indicative of a protocol deviation or safety event (or other noteworthy event as defined in the trial protocol)

Some priority datapoints are tightly controlled by the database and the user will not be able to save the CRF until this datapoint is completed (datapoint cannot be incomplete).

Other priority datapoints will have data validation checks run and/or source data verification (SDV) performed to confirm the data is complete, within an expected range, and/or have an associated safety or deviation event logged. These data validation and verification checks are conducted to ensure that any omissions or discrepancies in the data can be resolved as soon as possible, and prior to the interim scheduled analyses.

The table below shows the priority datapoints for the ROADMAP trial, and the type of priority they are given within the database.

Table 7 Priority Datapoints

Priority Datapoint Description	Datapoint Database Fieldname	Relevant CRF	Type of Priority (cannot be incomplete / validation check conducted / SDV performed)
Vital status at Platform Day 365	D365_VitalStatus	Day 365 CRF	Cannot be incomplete + validation check conducted + SDV performed
Date of death		Day 365 CRF	Cannot be incomplete + validation check conducted + SDV performed
Participant Consent		Platform Screening CRFs	Cannot be incomplete + SDV performed
Platform Eligibility Criteria		Platform Screening CRFs	Cannot be incomplete + validation check conducted + partial SDV performed

Participant Age/DOB & Sex		Platform Screening CRFs	Cannot be incomplete + SDV performed
Domain Eligibility Criteria		Domain Screening CRFs	Cannot be incomplete + validation check conducted
Participant Silo		Baseline CRF	Cannot be incomplete + validation check conducted + SDV performed
Acute Kidney Injury Safety Event – Derived Variable		Baseline CRF + Day 100 CRF	Validation check conducted
Acute Liver Injury Safety Event – Derived Variable		Baseline CRF + Day 100	Validation check conducted
C. difficile Safety Event – Derived Variable		Day 100 CRF	Cannot be incomplete + Validation check conducted
Change in Treatment Safety Event – Derived Variable		Day 100 and Day 365 CRFs	Cannot be incomplete + Validation check conducted
Protocol Deviations		Protocol Deviation CRFs	Validation check conducted

13.2.2 OTHER DATA CLEANING ACTIVITIES

As part of the Data Cleaning Reports, routine checks of common inconsistencies will also be performed. These checks relate to data fields that are of lower priority and are not important for the purposes of the interim analyses.

Throughout the lifetime of the trial, new inconsistencies may be picked up and incorporated into the reports. The reports are a working document that continue to change and grow as the database evolves.

For more information on what other checks are being conducted, please see the **Data Cleaning Report Template.**

13.3 DATA QUALITY QUERIES

Where possible, all data querying should be performed using the Monitoring system inbuilt within the Spinnaker database. The Monitoring tab displays a list of specific datapoint queries that have been raised by the regional managers, regional monitors, and/or data managers. These queries may be raised during a monitoring visit, as part of data cleaning, or during the participant locking process.

If a query cannot be entered within the database, it should be emailed through to the site, with specific reference to the database CRFs it relates to. A copy of the sent email should be kept as part of the TMF, and where possible, a query should also be added to the database to confirm the validity of the datapoint.

For more information on the inbuilt query system within the database, please view the **ROADMAP Spinnaker Video Guide.**

14 DATA ACCESS

Data access includes access to any trial data for the purposes of:

- Maintaining oversight of trial progress and management of the trial
- Conducting scheduled interim and final analyses of the trial data
- Providing datasets, upon request, to encourage collaboration and enhance value of the dataset

As a general policy, access to ROADMAP trial data for the above purposes is encouraged, but highly safeguarded.

- Prior to the publication of any trial results, as a default position, any post-randomisation data will not be accessed, except by the personnel conducting the scheduled analyses

- Access to personal data will not be permitted, unless required by law or regulatory request.

For more information on data sharing, please refer to the **Data Sharing Policy**.

14.1 ACCESS TO PERSONAL DATA

Personal data is any information that relates to an identified or identifiable living individual. Different pieces of information, which collected together can lead to the identification of a particular person, also constitute personal data. Any personal data collected or used in the course of the trial will be treated as confidential information at all times and will be stored securely with all security measures that would be necessary for compliance with data protection and GDPR.

14.1.1 PERSONAL DATA COLLECTED IN THE SPINNAKER DATABASE

Participant identifiers collected during screening (age/date of birth if applicable in the region) or later (sex at birth) will only be visible on-screen when viewing a participant record, or the list of participant records. Those with on-screen view of this information is limited to the site staff at that site, the RTMG, and the GTMG.

All participant identifiers are encrypted in the data exports and will not be accessible or visible in aggregate.

14.1.2 PERSONAL DATA COLLECTED FOR DATA LINKAGE

Additional identifiable data may be collected for the purposes of data linkage, in regions that are participating in data linkage and only for participants who specifically consent to this additional data collection.

This data will be kept on a separate secure REDCap database and will only be accessed by the site study staff at that site, and designated data coordinator(s) from the RTMG for the purposes of 1) providing the data for linkage, 2) the data linkage unit who will perform the linkage, and 3) regulatory authorities who may want to check that the study is being carried out correctly.

Table 8 Summary of Access to Personal Data

Role	Personal Data Collected in the Spinnaker Database	Personal Data Collected for Data Linkage
Analytic Team	*No access*	*No Access*
Data Safety Monitoring Committee (DSMC)	N/A	N/A
GTMG & RTMG	Visible On-Screen Only	*No Access*
GTMG – Data Coordinator(s)*	Visible On-Screen Only	**Accessible***
Site Staff	Visible On-Screen Only	**Accessible**
GTSC	-	-
Other Working Groups & Committees	-	-
*Only designated data coordinator(s) from the RTMG will have access to personal data for the purposes of providing data for linkage		

Please refer to the Region-Specific Appendix for further information about data linkage processes in each region.

14.2 ACCESS TO UNBLINDED DATA

Unblinded data comprises aggregate post-randomisation data (particularly that relating to the primary and secondary endpoints) stratified by allocated study treatments.

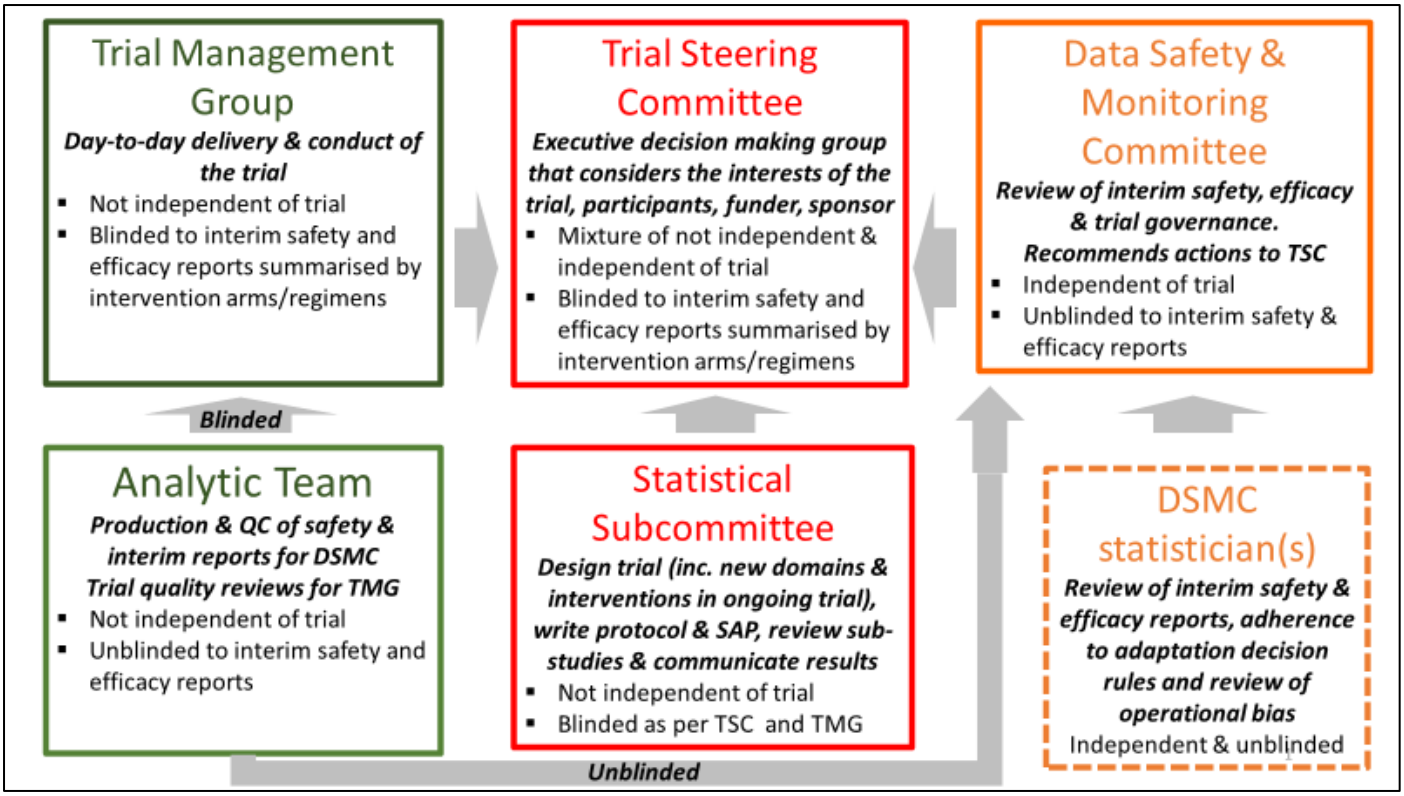

Figure 2 Simplified Flowchart of Unblinding in ROADMAP Trial

Prior to any domain, cell or trial conclusions, the only users with access to unblinded data will be the AT, and the data coordinator(s) from the GTMG, and the DSMC. Access is provided for the purposes of conducting the statistical analyses and producing the scheduled and final analysis reports required of the Bayesian Statistical Model.

Although the data coordinator(s) from the GTMG will have access to unblinded data, they will not have access to the unblinded (closed) reports produced by the AT as part of the scheduled analyses – only the AT and DSMC will have access to this level of unblinding.

Trial integrity demands clear delineation between those who have access to blinded and unblinded data and reports – the table below provides a summary of this access for each user group within the database.

Table 9 Summary of Access to Unblinded Data

Role	Blinding Status – Data	Blinding Status – Interim Reports
Analytic Team (AT)	**Unblinded**	**Unblinded**
Data Safety Monitoring Committee (DSMC)	**Unblinded**	**Unblinded**
GTMG & RTMG	Blinded	Blinded
GTMG – Data Coordinator(s)	**Unblinded**	Blinded
Site Staff	Blinded	Blinded
GTSC	*No access*	Blinded

Other Working Groups & Committees	*No access*	Blinded

Following the public release of any domain, cell or trial conclusions, access to unblinded data (including data included in the publication of the results) must be carefully considered to maintain trial integrity for remaining domains. For example, in the final analyses following a domain closure, treatment effects will be estimated with covariate adjustment and these covariates may include allocation status to interventions in other domains which have yet to close.

See the **Data Sharing Policy** for further detail.

14.3 DATABASE EXPORTS & DATA REPORTS

Database outputs, including exports and reports, are available within the database to support oversight, management and conduct of the trial and analyses.

- **Database Exports** = direct database outputs containing raw data that are available as comma-separated value (.csv) files.
- **Data Reports** = database outputs that are derived from raw data and may be viewable as an on-screen report or downloadable as a comma-separated value (.csv) file.

Database users will have varying access these outputs, as outlined in the ROADMAP Spinnaker Video Guide and below.

14.3.1 DATABASE EXPORTS

Database exports are available within the database to support global oversight, management and conduct of the trial and analyses. Data Exports are direct database outputs containing raw data that are available as comma-separated value (.csv) files.

- Data exports **containing aggregate or line listed primary outcome data (unblinded data)** will only be visible to the Data coordinators unblinded (DCO) and unblinded statisticians (UST) profiles and will be unavailable for other users.
- Data exports **containing line listed intervention allocation data (unblinded data)** will only be visible to the DCO and UST profiles (unblinded analytic team and data coordinators) and will be encrypted for all other users.
- Any data **exports containing participant identifiable data (date of birth and initials, if collected)** will be encrypted.

Data exports are only available to members of the GTMG and AT – the specific access to these exports will vary with each user profile type and is summarised in the table below.

Table 10 Database Export Summary

Export Name	Export Detail	Contains Intervention Allocation Data	Contains Aggregate Primary Endpoint Data	Contains Identifiable Data
Patient Eligibility & Enrolment				
Patient Eligibility	Screening data for all participants screened (including screen failures), and includes initial consent data	-	-	Encrypted
Domain A Surgical Eligibility	Screening data for all participants screened (including screen failures) for the Surgical domain.	Encrypted	-	-
Domain B Antibiotic Choice Domain Eligibility	Screening data for all participants screened (including screen failures) for the Antibiotic Choice domain.	Encrypted	-	-
Domain C Antibiotic Duration (Part A) One-Stage Eligibility	Screening data for all participants screened (including screen failures) for the Antibiotic Duration (Part A) Domain	Encrypted	-	-

Domain D Antibiotic Duration (Part B) Two-Stage Eligibility	Screening data for all participants screened (including screen failures) for the Antibiotic Duration (Part B) Domain	Encrypted	-	-
Participants Enrolled	Summary of all participants enrolled to the randomised platform, including domain and intervention allocations	Export only available to UST & DCO	-	-
Data Collection CRFs				
Consent	Consent for trial and registry participants	-	-	-
Consent (Regained Capacity)	Data export of all data fields within that CRF			
Baseline		-	-	-
Day 100		-	Export only available to UST & DCO	-
Day 365		-	-	-
Protocol Deviation	Data export of all protocol deviations logged within the database	-	-	-
Withdrawal (Trial)	Data export of all data fields within that CRF	-	-	-
Data Description – Full Export	A full list of all data fields, and the corresponding data validation and field logic	-	-	-
Registry				
Registry	Summary of all participants enrolled in the registry	-	-	-
Registry baseline	Data export of all data fields within that CRF	-	-	-
Registry Day 365		-	-	-
Registry Withdrawal		-	-	-

USC = Unblinded Statistician; DCO = Data Coordinator

14.3.2 DATA REPORTS

Database reports are outputs that are derived from raw data. Database reports will be made available to trial site and management staff to support regional and site level oversight, management and conduct of the trial.

These reports be minimised to operational reports to ensure trial integrity and will not contain aggregate primary outcome data or intervention allocation data.

These reports will also not contain any participant identifiable data. If required, identifiable information is viewable onscreen within each participant record.

Data reports are made available via the following methods:

- **Direct Database Reports** – viewable as an on-screen report and/or downloadable as a comma-separated value (.csv) file.
- **Compiled Database Reports** – created by the GTMG

Database users will have varying access these reports, as outlined in the ROADMAP Spinnaker Video Guide and below.

These reports may be shared with the ROADMAP Community (including site investigators and in public reports, where appropriate). The reports may include overall numbers of participants screened, enrolled in the registry or platform, and in each domain (and silo). If RAR is introduced, the number of participants allocated to each arm will become unavailable.

The tables below shows specific reports in the ROADMAP Trial; who the report is generated by; the primary and personnel responsible for each and; where applicable, a timeline for each.

Table 11 Data Report Summary

Report Name	Report Detail	Type of Report	Timescale
Direct Database Reports			
Enrolment Report		Direct	Ongoing *Available as an on-screen and downloadable report via Spinnaker at any time to the GTMG, RTMGs & sites.* • *Sites will have access only their own site,* • *RTMGs will have access to all sites in their region* • *GTMGs will have access to all sites*
Data Outside Expected Ranges Report		Direct	Ongoing *Available as an on-screen and downloadable report via Spinnaker at any time to the GTMG, RTMGs & Sites.* • *Sites will have access only their own site,* • *RTMGs will have access to all sites in their region* • *GTMGs will have access to all sites*
Data Completion Report		Direct	Ongoing *Available as an on-screen and downloadable report via Spinnaker at any time to the GTMG, RTMGs & Sites.* • *Sites will have access only their own site,* • *RTMGs will have access to all sites in their region* • *GTMGs will have access to all sites*
Site Location Settings & User Export		Direct	Ongoing *Available as a downloadable export via Spinnaker at any time to the GTMG & RTMGs.* • *RTMGs will have access to all sites and users in their region* • *GTMGs will have access to all sites and users*
Consent Withdrawals Report		Direct	Ongoing *Available as an on-screen and downloadable report via Spinnaker at any time to the GTMG, RTMGs & Sites.* • *Sites will have access only their own site,* • *RTMGs will have access to all sites in their region* • *GTMGs will have access to all sites*
Compiled Database Reports			
Simple Global CONSORT	Blinded to platform, domain exclusion summary details and intervention allocations	Compiled	Every 4 weeks *Will be made available to the ROADMAP Trial Community via email update*
Detailed Global CONSORT	Unblinded to platform and domain exclusion summary details, and intervention allocations	Compiled	Every 4 weeks *Will be made available to the RTMGs via email circulation*
Simple & Detailed Region-Specific CONSORT	Blinded/unblinded as per Global CONSORTs	Compiled	Every 4 weeks *Will be made available to the RTMGs via email circulation*
Hospital-Specific CONSORT	Unblinded to platform and domain exclusion summary details and intervention allocations	Compiled	Every 4 weeks *Will be made available to the RTMGs via email circulation*
Expected vs Actual Recruitment	Shows expected vs actual recruitment (based on actual data	Compiled	Every 4 weeks

	provided via survey) at a regional level		*Will be made available to the RTMGs via email circulation*
Protocol Deviations Export	Replication of the protocol deviations export at a regional level	Compiled	Ongoing *Will be provided by the GTMG to the RTMGs for their region until a downloadable export is available on the database.*
Consent Events Report	Replication of the consent events export at a regional level	Compiled	Ongoing *Will be provided by the GTMG to the RTMGs for their region until a downloadable export is available on the database.*
Screened Patients Report	Summary of all screen failures within a region	Compiled	Ongoing *Will be provided by the GTMG to the RTMGs for their region until a downloadable export is available on the database.*

15 DATA EXTRACTION & STORAGE FOR STATISTICAL ANALYSES

The Statistical Analysis Plans (SAP) will document the analysis requirements in detail. Statistical analyses will be performed using the unblinded data exports, extracted from the Spinnaker database at the timepoints outlined in the AT Terms of Reference. The Terms of Reference also contains confidentially clauses regarding access to the unblinded data.

When extracted, the exports will be downloaded to a local file temporarily before being immediately transferred to a ROADMAP-specific Research Data Share Drive (Research-NAS[CIFS])

The ROADMAP Research-NAS (CIFS) drive is a secure 1TB University of Newcastle Research Data Share Drive.

- It is a standard network file share that can be mounted onto a computer
- It is only accessible via the University network or via UoN VPN connection by university staff (or honorary appointees)
- Access is provided by the Research Computing Activity Owner (RCAO), who is the owner of the drive. The RCAO must be a permanent employee of the University of Newcastle.

Access to ROADMAP Research-NAS drive is limited to the members of the AT. The RCAO for this drive is the University of Newcastle appointed member of the AT.

All data exports that are extracted from the Spinnaker database by the AT will only be stored on the ROADMAP Research-NAS for the duration of the trial.

15.1 SCHEDULE OF KEY EXTRACTION EVENTS

Table 12 Schedule of Key Extraction Events

Analysis	Milestone	Participant Recruited	Participant Reaches D100	Data Extraction by ROADMAP-AT	Report Provided to DSMC
Scheduled Interim Analyses					
Analysis 1	500th participant				
Analysis 2	1,000th participant				
Analysis 3	1,500th participant				
Analysis 4	2,000th participant				
Analysis 5	2,500th participant				

Final Analyses					
Domain Analysis	Last participant recruited to a domain				
Sub study Analysis	Last participant recruited to sub study				
Final Analysis	Last participant recruited to the platform				

15.2 SCHEDULED ANALYSES

Scheduled analyses will be performed by the ROADMAP Analytic Team (AT) upon each 500th platform participant reaching day 365. For analyses involving the primary endpoint of 365-day mortality, only those participants where 365 days have elapsed since platform entry will be included. i.e., participants who have died, but where 365 days have not elapsed since platform entry will not be included.

The *a priori* statistical instructions for each scheduled analysis will be documented in the Statistical Implementation Guides (SIG), produced by the blinded members of the Statistical committee. The SIG will be version controlled, with a new version produced for each scheduled analysis, incorporating any changes or new information that the AT requires to conduct the analysis. The SIG will be made publicly available via the ROADMAP website prior to each scheduled analysis.

The GTMG will provide email confirmation to the AT that the data is ready for extraction and confirm the date by which the data extraction should be completed.

15.2.1 DATA QUALITY CONTROL & QUERY RESOLUTION FOR SCHEDULED ANALYSES

As per the timelines specified in the Analytic Team (AT) Terms of Reference, there will be a period of time between the participant reaching day 365 and the extraction date, where the GTMG and RTMGs will finalise outstanding data quality control checks relating to the Priority Datapoints (see Table 7).

As part of each scheduled analysis, the AT will also perform routine quality checks on the data. They may also choose to extract data from the staging environment to conduct test analyses (with dummy data) to develop and check code, and to ensure the necessary fields are available for the scheduled analyses.

The GTMG-Data Coordinator(s) will work with the AT to resolve any concerns or issues with the data. All emails between the GTMG-Data Coordinator(s) and the AT that discuss the unblinded scheduled interim analysis data will have the email subject: "CONFIDENTAL ROADMAP TRIAL INTERIM RESULTS" and will not be included in the ROADMAP Trial Master File (TMF). If any files are shared that contain unblinded trial data, they will be password protected.

15.2.2 PRODUCTION OF THE OPEN AND CLOSED REPORTS

The AT will be responsible for producing both the open (blinded) and closed (unblinded) scheduled analysis reports, as per the timelines specified in the ToR.

- **Closed Report (blinded):** will only be reviewed by the DSMC
- **Open Report (unblinded):** will be reviewed by the GTSC and GTMG and can be accessed by the RTMGs in order to complete region-specific reporting requirements. These reports will not be shared outside of these groups, unless specified or requested by the GTMG.

15.3 FINAL ANALYSES

Final analyses will be performed by the AT when a domain, cell or the trial as a whole has reached a conclusion, as per the prespecified stopping rules in the Core Protocol.

The *a priori* statistical instructions for the final analyses will be documented in the SAP produced by the blinded members of the Stats-WG. The SAP will be version controlled, if any changes are made prior to the final report being produced. The SAPs will be made publicly available via the ROADMAP website prior to each final analysis.

The GTMG will provide email confirmation to the AT that the data is ready for extraction and confirm the date by which the data extraction should be completed.

If other aspects of the trial are still open, the trial will continue to accrue data, however, further enrolment into the relevant aspect (domain, silo, etc.) that is undergoing final analysis will be prohibited within the database.

15.3.1 DATA QUALITY CONTROL & QUERY RESOLUTION FOR FINAL ANALYSES

Final analyses will be conducted when the GTMG have confirmed that all queries are resolved, and the data is verified as complete for the relevant datapoints. Participant records that form part of a final analysis will be *soft locked* prior to the analysis occurring (see Section 17.1); the database exports used for the final analysis will serve as the locked analysis dataset. As these participants may also form part of another final analysis, the data may be unlocked and updated as part of subsequent data quality control. Participants will be *hard locked* prior to the final analysis of the trial as a whole (see Section 17.2).

As part of the final analysis, the Analytic Team (AT) will perform routine quality checks on the data. They may also choose to extract data from the staging environment to conduct test analyses (with dummy data) to develop and check code, and to ensure the necessary fields are available for the analyses.

The GTMG-Data Coordinator(s) will work with the AT to resolve any concerns or issues with the data. All emails between the GTMG- Data Coordinator(s) and the AT that discuss the unblinded final analysis data will have the email subject: "CONFIDENTAL ROADMAP TRIAL RESULTS" and will not be included in the ROADMAP TMF. If any files are shared that contain unblinded trial data, they will be password protected.

15.3.2 PRODUCTION OF THE FINAL REPORTS

The AT will be responsible for producing the final reports. These reports will be shared with the GTMG, GTSC, Stats-WG and any other relevant working groups who may be involved in producing the final manuscript. These reports will only contain primary, secondary and safety outcome data relevant to that analysis; whole-trial outcome data will remain blinded until the trial as a whole is concluded.

15.4 SUB-STUDY ANALYSES

Various sub-studies may be incorporated into the ROADMAP Trial throughout the lifetime of the study.

Sub-study analyses will be performed on data already collected for the ROADMAP Trial and/or additional sub-study-specific data collected either within the Spinnaker database or externally. Unless otherwise agreed upon, sub-study analyses typically will not be performed by the AT; but instead by the sub-study lead, sub-study working group, or an external nominated statistician. The *a priori* statistical instructions for the sub-study analyses will be documented in the sub-study protocols.

The GTSC will provide approval of ROADMAP trial data extraction, via the **Data Access Request Process**. As a general rule, sub-study analyses will not occur prior to the analysis and publication of the ROADMAP Trial results; exceptions may be made by the GTSC on a case-by-case basis, if the publication will not compromise trial integrity. See the **Authorship & Publication Policy and Data Sharing Policy** for further detail.

Where sub-study data extraction has been approved, the GTMG will liaise with the sub-study lead(s) to organise relevant data export access. The AT will also be notified of the sub-study analysis.

A full record of all data extractions will be maintained by the GTMG.

15.4.1 DATA QUALITY CONTROL & QUERY RESOLUTION FOR FINAL ANALYSES

Final analyses will be conducted when the sub-study lead has confirmed that all queries are resolved, and the data is verified as complete for the relevant datapoints; it will be the full responsibility of the sub-study lead(s) to ensure that all relevant quality control checks have been completed prior to sub-study analysis.

If the sub-study is using ROADMAP Trial data, the GTMG-Data Coordinator(s) will work with the sub-study lead(s) to resolve any concerns or issues with the data. All emails between the GTMG-Data Coordinator(s) and the sub-study leads that discuss unblinded data will have the email subject: "CONFIDENTAL ROADMAP TRIAL RESULTS" and will not be included in the ROADMAP TMF. If any files are shared that contain unblinded trial data, they will be password protected.

15.4.2 PRODUCTION OF THE SUB-STUDY REPORTS

The sub-study lead(s) will be responsible for producing the sub-study reports.

15.5 EXTERNAL DATA THAT SUPPORTS THE ANALYSES

Spreadsheet logs are maintained by the GTMG electronic Trial Master File (eTMF) to log information that is not available to be recorded within the Spinnaker database. These logs are outlined in the table below:

Table 13 Spreadsheet Logs Maintained in the Electronic Trial Master File (eTMF)

Database Log Name	Description
Data Corrections Registers	Data collected during platform and domain eligibility screening that cannot be edited by sites requires corrections to be made by the database developer (Spiral). A summary of the correction is recorded in this log. File tag numbers link to an Evidence Archive of correspondence, containing other details related to each correction. Includes additional datapoints that were found to be missing during data cleaning checks and were collected externally to the database.
Data Integration/Collection Logs	These logs summarise the data recorded on paper CRFs and reported to the central team whilst the electronic reports in Spinnaker (trial database) were under development. Once implemented, the information is retrospectively entered into the database and the log is archived. Includes: • Silo discrepancies log • Safety events log • Protocol deviations log • Other data collections log

16 DATABASE LOCK

Participant records that form part of a final analysis will be locked before the analysis is conducted. For a participant record to be locked, the GTMG and RTMGs will ensure that data cleaning is complete and data quality control conditions have been met.

As there will be multiple final analyses that are conducted for the ROADMAP Trial, there will be two stages of database lock:

1. **Soft Lock of Participant** – *occurs when one or more final analyses for a domain/trial aspect is conducted*
   Participant records relevant to an analysis will be locked once data cleaning and quality control has been undertaken. These records may be unlocked, and data updated, if new information is discovered or new queries are generated as part of a subsequent analysis. This will be in the form of a data cut.

2. **Hard Lock of the Database** – *only occurs when the final analysis of the trial is conducted, and the whole-trial outcome data is reported*

The database will undergo a final round of cleaning and quality control. Once the hard lock is applied, no further changes to participant data can be made.

Please see the ROADMAP Spinnaker Video Guide for further detail on the operationalising of data locks within the database.

16.1 SOFT LOCK OF PARTICIPANT RECORDS

Soft lock of the participant records will occur when one or more final analyses for a domain/trial aspect is conducted. Only the participant records relevant to that analysis will be required for soft lock.

Participant records will be soft locked once data cleaning and quality control has been undertaken. These records may be unlocked, and data updated, if new information is discovered or new queries generated as part of a subsequent analysis. The GTMG and RTMG will retain access to soft lock and unlock for these participant records.

The procedure for soft lock of the participant records will commence once the following data quality conditions have been met:

- All relevant participant eligibility screening data is 100% complete
- All relevant participant consent has been SDV'd.
- All Priority Datapoints (see Table 7) relevant to the analysis have been validated
- All relevant data cleaning queries are resolved
- All relevant participant CRFs are complete or have a data override performed
- All relevant participant PDCs have been entered into the database
- All relevant participant data corrections have been actioned by the database provider (Spiral)

Data quality will be improved using the methods outlined in Sections 14 and 16 and repeated until the above conditions are met.

The database exports used for the final analyses will serve as the locked analyses dataset.

16.2 HARD LOCK OF THE DATABASE

Hard lock of the database will only occur when the final analysis of the trial is conducted, and whole-trial outcome data is reported.

As a locked database should only be updated in extraordinary circumstances, comprehensive efforts will be made to ensure that data is as clean as possible with each final analyses conducted prior.

The procedure for hard lock of the database will only commence once all the following data quality conditions have been met:

- All participant platform and domain eligibility screening data are 100% complete
- All platform participant consent has been SDV'd
- All monitoring visits have been completed and queries resolved
- All Priority Datapoints (see Table 7) have been validated
- All data cleaning queries are resolved
- All platform CRFs are complete or have a data override performed
- All Protocol Deviation and Safety Report CRFs have been entered into the database
- All data corrections have been actioned by the database provider (Spiral)

Data quality will be improved using the methods outlined in Sections 14 and 16 and repeated until the above conditions are met.

Once the data quality conditions have been met and documented, a Database Lock Request Form will be completed by the AT and GTMG and submitted to the database provider. The database provider will then hard lock the database as per the signed Service Agreement and SoW.

17 DATABASE ARCHIVING

Once the study is completed, and it has been determined that no further access is required, the GTMG will ensure the following tasks are completed in accordance with ICH-GCP:

- The trial database is archived (completed in conjunction with the database provider)
- Data exports saved to the ROADMAP Research-NAS drive, are archived (completed in conjunction with the AT)
- All relevant database paper documentation (paper CRFs, etc.) are archived in the TMF.

Prior to archiving the database, each study site will be provided with electronic copies of the CRFs for each participant recruited at their site. These should be archived as per ICH-GCP, and in accordance with regional and local archiving procedures.

18 APPENDIX 1: RECORD OF CHANGES

VERSION NUMBER	DATE	SECTIONS AFFECTED	SUMMARY OF CHANGES	AUTHOR INITIALS