SNAP Trial Integrity Suite:

Study Proposal Guidance Document

DOCUMENT APPROVAL

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The SNAP Global Trial Steering Committee (GTSC) and Regional Trial Management Groups (RTMGs) have had the opportunity to review this document, and it has been signed by the Chief Investigators and the Chair of the GTSC on behalf of the SNAP Trial.

IF ADAPTING THIS DOCUMENT, PLEASE ACKNOWLEDGE US VIA THE FOLLOWING STATEMENT:

"This document has been adapted from the *Staphylococcus Aureus* Network Adaptive Platform (SNAP) Trial Integrity Suite: Governance & Management Overview (Version 2.0), available from the SNAP Trial website: https://www.snaptrial.com.au/for-investigators#integrity.

The SNAP trial, globally coordinated by the University of Melbourne, is an international adaptive platform trial aimed at identifying the most effective treatments for *Staphylococcus aureus* bloodstream infections."

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2 SNAP TRIAL INTEGRITY SUITE

The SNAP Trial Integrity Suite is a comprehensive collection of essential documents that provide evidence and guidance for the conduct and oversight of the global SNAP Trial and sets the minimum standards of compliance for the study.

The SNAP Trial Integrity Suite is comprised of the following documents:

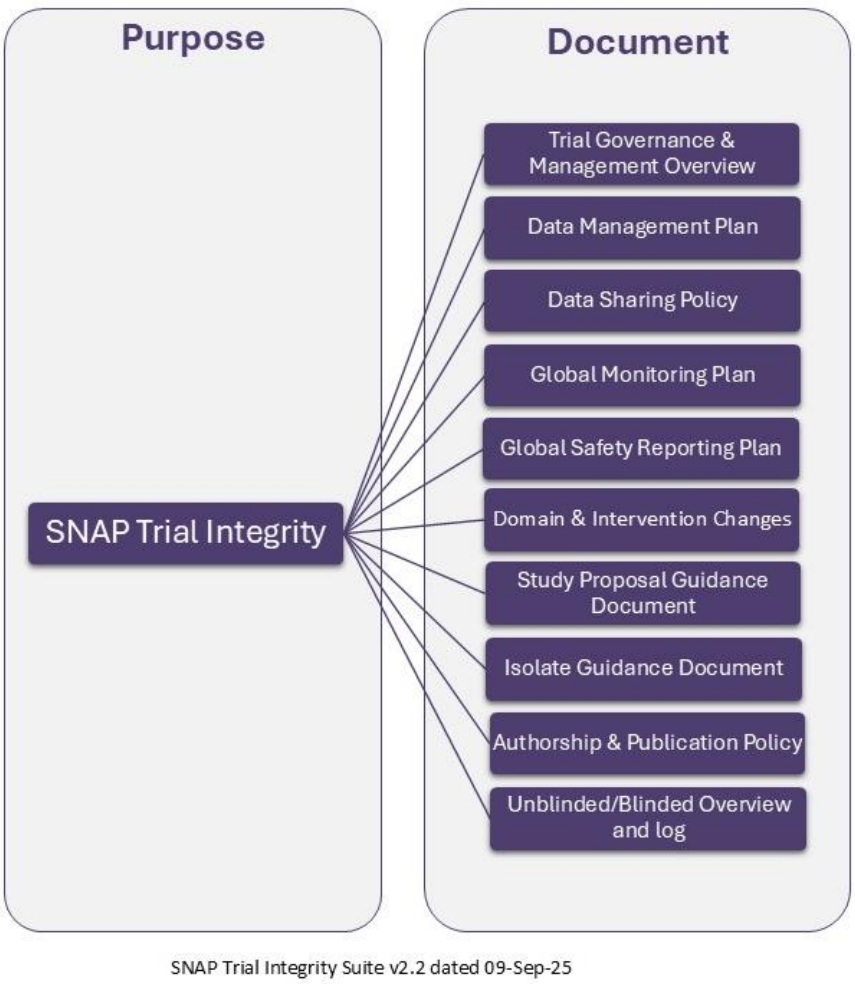


Figure 1 Trial Integrity Suite

3 INTRODUCTION

The infrastructure and data collected in the SNAP Platform and the associated SNAP Registry are a rich resource for new domains, nested trials, prospective sub-studies and secondary/exploratory analyses. This guidance document outlines the requirements and processes for the application and integration of new research proposals to the SNAP Trial. This includes a review by the SNAP Design Working Group, ratification by the Global Trial Steering Committee (GTSC), and the subsequent ethics approvals and data access requirements for integration into the SNAP Trial infrastructure. New research proposals should be submitted to the SNAP trial prior to the submission of any grants/funding applications to ensure they align with the SNAP trial goals and objectives.

This document also discusses the key aspects to consider when submitting a research proposal for review, including the criteria for review, database and statistical model integration, data access and release considerations, and other things to consider prior to submitting a proposal for review.

The ongoing and adaptive nature of the SNAP trial means that extreme care is required before releasing any participant data from the database, even for relatively small projects.

See the following documents on the SNAP website for more information about data access and sharing for SNAP studies:

- Data Sharing Policy
- Authorship and Publication Policy
- Data Management Plan
- Isolate Guidance Document

If you have further questions about the proposal review process, please contact the SNAP Global Trial Management Group (GTMG; snap-trial@unimelb.edu.au).

4 DEFINITIONS

The definitions relevant to the proposal process for the SNAP Trial are defined below. All definitions will be referenced by their acronyms throughout this document.

Table 1 Relevant Terms

Term	Description
Global Trial Steering Committee (GTSC)	The global steering committee responsible for overall decision making related to the SNAP trial.
Independent Ethics Committee (IEC)	An independent body (a review board or a committee, institutional, regional, national, or supranational), constituted of medical professionals and non-medical members, whose responsibility it is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial and to provide public assurance of that protection, by, among other things, reviewing and approving/providing favourable opinion on, the trial protocol, the suitability of the investigator(s), facilities, and the methods and material to be used in obtaining and documenting informed consent of the trial subjects. The legal status, composition, function, operations, and regulatory requirements pertaining to Independent Ethics Committees may differ among countries but should allow the Independent Ethics Committee to act in agreement with GCP as described in this guideline.

Institution / Trial Site	Any public or private entity where clinical trial-related activities are conducted
Institutional Review Board (IRB)	An independent body constituted of medical, scientific, and non-scientific members, whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trial protocol and amendments and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects.
Regulatory Authorities	Bodies having the power to regulate. In the ICH GCP Guideline, the expression Regulatory Authorities includes the authorities that review submitted clinical data and those that conduct inspections. These bodies are sometimes referred to as competent authorities.
Sponsor	An individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial in a given region.

5 PROPOSAL CATEGORIES

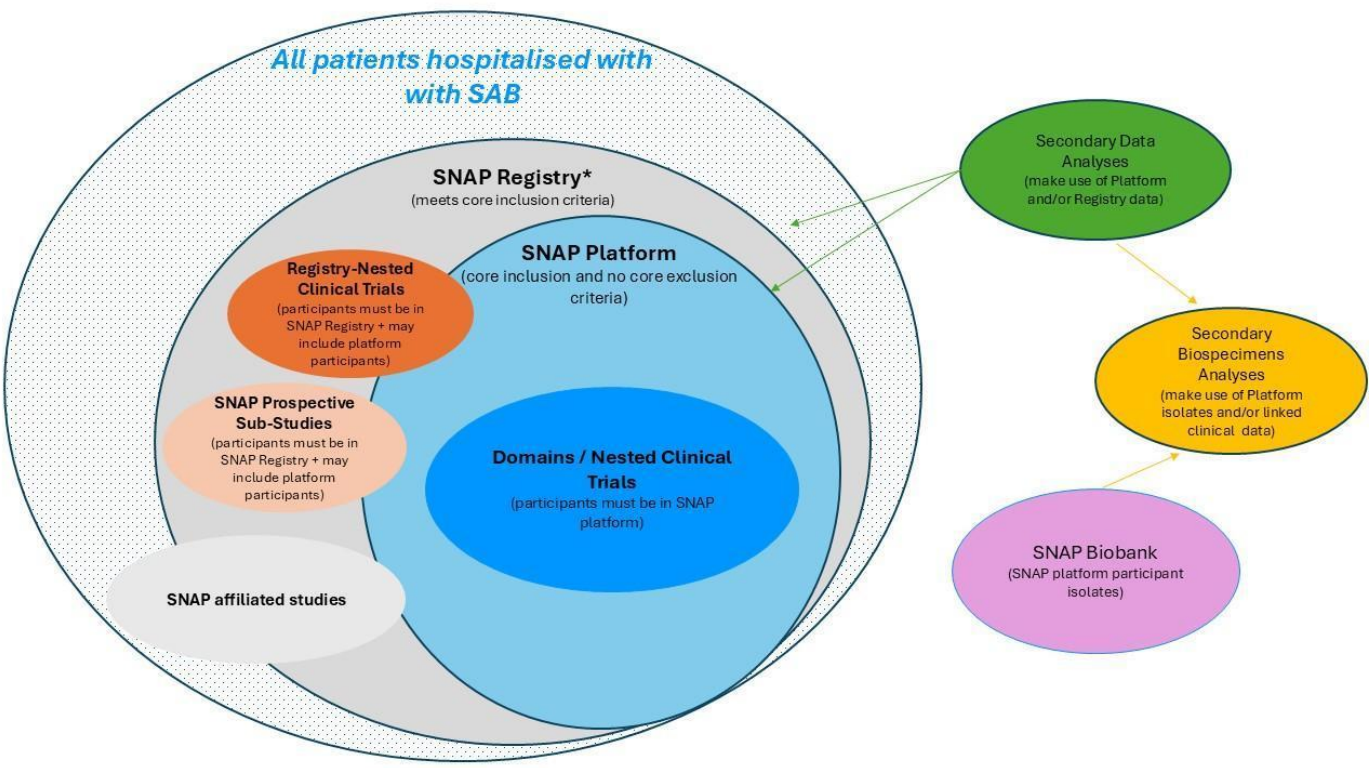


Figure 2 Proposal Categorisation Diagram

Proposals will be categorised as:

1. **Platform-Nested Clinical Trial**
   (Includes new domains, new interventions within a domain, and other clinical trials that sit within the core randomised platform)
   Proposals that fall under this category meet the following criteria:
   - Involve randomisation
   - Must include only participants who are eligible for and enrolled into the core platform
   - Uses existing SNAP core protocol and infrastructure but is not restricted to the core primary endpoint

- Preferred approach is to use existing SNAP statistical appendix and statistical model, but may use a separate statistical approach if needed

Proposals that fall under this category will require SNAP-templated protocols, ethics, consent and likely additional funding. These proposals may use their own electronic data capture (EDC) system but should make use of the core randomisation module in the Central Spinnaker EDC, unless otherwise justified and approved by the GTSC.

Full proposal review process will need to be completed (see Section 6).

2. **Registry-Nested Clinical Trials**

(Includes new domains and other clinical trials that sit within the registry)

Proposals that fall under this category meet the following criteria:

- Involve randomisation
- Must include participants who are eligible for and enrolled into the registry, but can also include participants who are enrolled into the core platform
- May (but not required to) use existing SNAP statistical appendix and statistical model

Proposals that fall under this category will require SNAP-templated protocols, ethics, consent and likely additional funding. These proposals may use an EDC of their choice.

Full proposal review process will need to be completed (see Section 7).

3. **Prospective Sub-Studies**

(Includes studies that collect data/samples additional to what is outlined in the core/registry protocols)

Proposals that fall under this category meet the following criteria:

- Do not involve randomisation
- Must include participants who are eligible for and enrolled into the core platform, but can also include participants who are enrolled into the registry
- Includes collection of samples and/or clinical data from SNAP platform and/or registry participants above what is outlined in the core and/or registry protocol

Proposals that fall under this category will require SNAP-templated protocols and, ethics review and approval. Additional consent for the prospective study procedures and additional funding (which may be provided in-kind by proposal lead) is likely required. These proposals may use an EDC of their choice.

Full proposal review process will need to be completed (see Section 7). If the prospective sub-study will only be available in one country, the proposal will be reviewed by the Regional TMG and approved by the RTSC for that country, instead of the Design Working Group (WG) and GTSC.

4. **Secondary Data and/or Biospecimen Analyses**

Includes:

a) New analyses using existing SNAP Trial data which are not already described in existing approved SNAP protocol documents and/or
b) New microbiological analyses using SNAP Trial bacterial isolates and/or the isolate phenotypic/genotypic data.

These requests require the submission of an Expression Of Interest (EOI) for ratification by the GTSC (or RTSC where only one country/regions data/isolates are requested). Upon ratification,

a Data Access Request Form and/or an Isolate Access Request Form will need to be completed and submitted alongside the final protocol.

See section 10 for further information.

6 STUDY PROPOSAL REVIEW CRITERIA

Proposals will be judged on the following criteria for integration into the SNAP Trial.

- **Trial Integrity**
  Does this study require access to data that could threaten trial integrity? Does this study wish to report on trial outcomes prior to the SNAP Trial Results paper?

- **Harmony with SNAP Protocols**
  Does the study require a significant amount of data/sample collection outside of standard care or SNAP trial protocols? Are the sample/data collection harmonised with the SNAP trial protocols and other current domains/nested studies/sub-studies?

- **Adoption of the Pragmatic Trial Approach**
  Does this study place a significant additional burden on the participant or the site study team? Does the proposal include only the necessary data collection to answer the research question?

- **Feasibility**
  Is the sample size reasonable and achievable? Will the research question be able to be answered recruiting only SNAP Trial participants?

- **Global Application**
  Has the investigator considered the ability for the proposal to be conducted in other regions/countries? Is the proposal applicable to other countries/regions?

- **Paediatric & Pregnancy Involvement**
  Has the investigator considered the involvement of children and pregnant patients? If not involving these participants, has this been sufficiently justified?

- **Funding**
  Has funding for this proposal been considered or obtained? Are there any grants the investigator is intending to apply for to cover the costs of the proposal? Has a proposal been put forward to the GTMG for financing the integration of this proposal into the SNAP Trial Infrastructure?

- **Sample Collection, Analysis & Shipping**
  Will samples be collected for this study and shipped to an external location? Has the shipping and storage of these samples been considered? Has a plan for the analysis been generated?

- **Integration with the Statistical Model**
  Will this proposal require integration into the overall SNAP statistical model? Who will be conducting the statistical analyses?

- **Integration with the SNAP Electronic Data Capture Systems (EDCs)**
  Will this proposal require integration into the existing SNAP Trial EDCs and/or existing randomisation modules?

- **Integration with the existing Data and Safety Monitoring Committee structure**
  Will this proposal require DSMC oversight? What will be the lines of reporting to the DSMC?

7 STUDY PROPOSAL REVIEW PROCESS

The SNAP Design Working Group (WG) will review all nested clinical trial proposals, and sub-study proposals involving two or more countries, to determine if they are suitable for the SNAP Trial. The proposals will be judged on the criteria described in Section 6, as well as overall scientific merit. Note that the role of the design working group is to help investigators refine their proposals so they will work with the overall SNAP machine/infrastructure, not to approve or deny a proposal. The GTSC is the decision-making body, and the design WG advises the GTSC.

Nested Clinical Trials and Sub-Study Proposals will be judged in 2 stages:

1. **Expression of Interest** (EOI) – the EOI will be reviewed by the Design WG and their recommendation will be provided to the GTSC.
2. **Full Protocol** – the full protocol will be reviewed by the Design WG in detail. The final protocol will be presented by a Design WG member at the next GTSC meeting for ratification.

At each of these stages, the Design WG will be provided the opportunity to raise questions and comments for the study lead(s) to respond to, prior to proceeding to the next stage. All comments/questions will be returned to the proposal lead(s) within two weeks of the Design Working Group review.

Please see **Appendix 2 below for a flowchart overview of the study proposal process*

7.1 EXPRESSION OF INTEREST

An EOI is the first stage of the review process for **all** proposals (including secondary analyses). This simple outline will be assessed for scientific merit (including significance and impact, and quality of methods) and feasibility (including available support, sample size, data collection methods, and funding). The EOI will be reviewed by at the next suitable meeting (or out of session), and any comments or questions will be returned to the study lead(s).

The Design WG will provide a recommendation for:

- The proposal to proceed to full protocol
- The proposal lead(s) to revise the EOI & provide a response to queries raised by the Design WG
- The proposal not to proceed further, as deemed unsuitable for the SNAP Trial at this time

A complete list of all EOIs received and the Design WG recommendations will be provided in the GTSC minutes and agendas.

7.2 FULL PROTOCOL

The Full Protocol is the final stage of the review process. This is the SNAP-templated final document outlining the design of the study proposal, and describes the objectives, methodology and overall organisation of the research to be carried out within the SNAP Trial infrastructure. This protocol will be submitted for ethical review in all participating countries and will be provided to participating sites to conduct the study. The Design WG will work with the study leads to ensure that the proposal can be feasibly operationalised.

The full protocol will be discussed at the next suitable Design WG meeting, and a recommendation will be made to the GTSC to ratify the protocol. The GTSC are the decision-making body and will have the opportunity to return comments for amending the protocol prior to operationalisation.

At the next available GTSC meeting or out-of-session communication, the committee will provide a consensus vote for:

- The protocol to be ratified with no further queries
- Request for a revised protocol & response to queries raised by the GTSC
- The study proposal to be rejected

7.2.1 STUDY PROPOSAL OPERATIONAL PROFORMA

Study leads will be required to complete an Operational Proforma alongside the full protocol outlining the following:

- Statistical design and analysis plans
- Data collection methods, tools, and schedules.
- Resource requirements (e.g., personnel, equipment, funding)
- Plans for data management, privacy protection, and confidentiality.
- Timeline and milestones for the study.
- Budget and funding sources for the study.

7.3 ADDITIONAL WORKING GROUP REVIEW

If required, the study protocol will undergo further review from additional working groups, including but not limited to:

- **Microbiology WG**
  Proposals involving isolates, or the microbiological aspects of the SNAP Trial.

- **Statistics WG**
  Proposals that intend to use the SNAP statistical model or may impact the statistical model.

- **Relevant Domain-Specific WG(s)**
  Proposals that are nested within, or will have an impact on, a particular domain.

- **Paediatrics and Pregnancy WG**
  Proposals that intend to enrol paediatric or pregnant participants.

- **Health Economics WG**
  Proposals that intend to collect additional health economic data.

- **Regional Consumer Reference Group or PPI WG**
  Proposals that require additional consent occurring in that region.

- **SNAP Regional Trial Management Groups**
  Proposals that require regional approval and oversight.

7.4 REVIEW OUTCOMES

The outcome of the review process will be communicated to the lead(s) by the SNAP GTMG.

A list of all approved proposals and their status will be available on the SNAP Website: https://www.snaptrial.com.au/substudies.

7.4.1 GTSC RATIFICATION

When a study proposal is recommended by the Design WG and ratified* by the GTSC, a formal email will be provided to the lead(s), including the appropriate RTMGs, informing them of this outcome.

This ratification may come with TSC comments/queries that will need to be addressed prior to proceeding with the proposed sub-study.

7.4.2 Period of Ratification

Once ratified by the GTSC, the ratification will be valid for a period of 12 months.

If no progress on the proposal has been made during the 12-month period, the protocol will need to be resubmitted to the Design WG to ensure the priorities and feedback provided are still applicable within the current trial landscape.

Once re-submitted, it will go through the normal process for GTSC review and be ratified or recommended not to proceed at this time.

7.4.3 Proposal Not to Proceed

If the Design WG and/or GTSC feel the proposal is not suitable for integration within the SNAP Trial, the lead(s) will be formally notified by email that the proposal has not been approved.

A proposal may not be approved to proceed if, for example:

- The proposal would be better as a standalone study, but which may be able to co-enrol (see Appendix 3) and/or perform a meta-analysis with SNAP
- A similar or identical proposal is already planned or in progress. In this case, the proposal lead(s) would be encouraged to collaborate on the planned trial integration.

8 Ethical & Regulatory Approval (For Ratified Proposals)

Ethics approval is generally required when conducting research projects that involve human participants and/or their data, including secondary use of existing data. In certain cases, research can be exempted from the requirement to seek ethical review – the specific criteria and processes for obtaining an exemption may vary across jurisdictions. In general, exemptions can be applied to:

> *1) secondary use of existing data for purposes considered within the scope of understanding staphylococcal infections*
>
> *2) data that is provided in a manner which is de-identified not re-identifiable, and*
>
> *3) participants have consented to the future use of their data for research related to staphylococcal infections*

The sections below outline the specific ethics and regulatory requirements for proposals that go through the full SNAP review process.

These documents will need to be prepared and collated for ethics and institution submission (where applicable in each region) and will be provided to participating sites who have opted to participate in the ratified proposal.

Each ratified proposal may require additional regulatory review and approvals. These additional reviews may include:

- National regulatory/governing bodies (for example, TGA)
- Lead ethics review in each region/country in which the ratified proposal will be made available
- Local institutional ethics review at each site that will be participating in the ratified proposal.

The proposal lead(s) in collaboration with the Design WG and SNAP RTMGs will be responsible for checking which reviews are required in each region that is participating.

8.1 Document Preparation

The following documentation may be required for a ratified study proposal. Template documents are available from the SNAP GTMG. Please reach out with any questions you may have about whether these documents are required for your ratified proposal.

- **Patient Information**
  Ratified proposals that include tests, procedures, sample collection, or data collection that are *additional to the SNAP Trial or to standard of care procedures* will require a separate Participant Information Sheet (PIS) or Participant Information Sheet & Consent Form (PICF) to be provided to eligible participants.

  In jurisdictions where the simplified layered consent model has been approved, a simplified PIS may be used. This simplified PIS will contain a brief overview of the ratified proposal, including a summary of *any tests, procedures, sample collection, or data that is additional to the SNAP Trial or standard of care procedures*, and a synopsis of the shipping or storage of samples external to the SNAP protocols.
    - This document should reference the SNAP Website and will provide a direct link for the participant to read more information if they wish.
    - This template will be provided by the GTMG to the proposal lead(s) for completion.

  A template simplified PIS has been created for adaptation. Please contact the SNAP GTMG to discuss this further.

  **Please note:* *Not all regions will be able to use the simplified model of consent, and this can be discussed further on a case-by-case basis.*

- **Website Information**
  For approved Platform- and Registry-Nested Trials and Prospective Sub-studies, each lead(s) will be required to provide additional information for the SNAP website available here: https://www.snaptrial.com.au/substudies
    - This website information will be used to document all active and approved proposals embedded within the SNAP Trial in one central location.
    - The website information can also be used to provide more in-depth information about each ratified proposal for the participant, if they choose to seek out further detail. This website information will be used for participants in regions that have approved use of the simplified consent model.
    - The study lead(s) will also have the option to provide an **additional short video** to summarise the proposal, at the expense of the study proposal lead. This video will be displayed with the information on the website.

  A template website information form will be provided by the SNAP GTMG to the proposal lead(s) for completion.

8.2 Ethical Review

Where ethical review of the proposal is required or exempt, the proposal lead(s) in collaboration with the Design WG and SNAP GTMG, will be responsible for:

- Ensuring that ethical review or exemption is received by each regional ethics committee, as required
- Liaising with the SNAP GTMG and RTMGs to prepare the required documents for submission
  Documents for submission may include:
    - Final Protocol – *ratified by the GTSC*
    - Final PIS/PICF(s) and Website Information – *confirmed by the SNAP GTMG and RTMG(s)*
    - If the ratified proposal will be **implementing interventions, procedures, or treatments** that are additional to the SNAP Trial protocols, further documentation for ethical review may be required. Please contact the SNAP GTMG to discuss further.

8.3 Institutional Review

A local institutional submission may be required in order for a site to participate in the ratified study proposal. Again, depending on the nature of the study proposal, this approval may be separate to the SNAP trial or may sit within the overarching institution approval of the SNAP Trial at the site.

If institutional review of the study proposal is required, the study lead(s) will be responsible for:

- Ensuring that institutional reviews are conducted at each participating site, as required
- Liaising with the SNAP GTMG and RTMG to prepare the required documents for submission
  Documents for submission may include:
    - Approval Letter & Associated Documents– *approved by the region-specific ethics committee*
    - Updated SNAP Trial Documents – *if applicable; updated to include the sub-study*
    - Localised study PIS/PICF(s) and Website Information – *if applicable; for the study and site*
    - Site-Specific documents such as departmental approvals, radiation reports, etc. – if any additional procedures/interventions/tests are required as a result of the study

The study will only be activated at each site once the institution has provided authorisation.

8.4 Agreements & Contracts

There are a few agreements that may be required for your study proposal. Template agreements are available from the SNAP GTMG and/or RTMG. Please reach out with any questions you may have about which agreements are applicable to your study.

- **Sub-Study Agreement – *between sub-study lead(s) and sponsor(s)***
  This agreement will outline any additional sample collection/transfer, data access/transfer, and publication and payments that will be involved with the conduct of this sub-study within the SNAP Trial. Each sub-study will be required to complete this agreement prior to proceeding with any sub-study activities, and this agreement will be fully executed as part of the ethical review process.

- **Site-Specific Contracts/Contact Updates – *between participating site(s) and the relevant regional sponsor(s)***
  Each participating site will need to have their site-specific research agreement updated to reflect any changes to the conduct of the SNAP Trial at their site, as a result of their participation in one or more sub-studies. This updated contract will include any additional payments provided to the site, outline any additional sample or data collection obligations, and any additional intervention, procedure, or departmental commitments that will be required. Each site will be required to accept this updated agreement prior to proceeding with any sub-study activities, and it will be fully executed as part of the institution approval process.

- **Data/Material Transfer Agreement – *between study lead(s) and the SNAP data custodian(s)***

If a Data Access Request Form or an Isolate Request Form is submitted, a data or material transfer agreement will be required at the time of data or isolate handover. This is an agreement between two or more entities (most likely legal entities) that are providing and receiving data or materials. It specifies the conditions under which the data or materials will be shared and documents what can and cannot be done with the data or materials, giving clarity and certainty to all parties.

8.5 Registration of Study Proposals

ClinicalTrials.gov is a website and online database of clinical research studies and information about their results. The purpose of ClinicalTrials.gov is to provide information about clinical research studies to the public, researchers, and health care professionals.

All studies involving randomisation in the SNAP trial should be registered on clinicaltrials.gov by the study lead as a separate listing, and should reference the SNAP Trial (NCT05137119) in the sections as below:

- **Brief Summary**
  Please include the following sentence: *"This study is an approved [domain/nested trial/prospective sub-study] of The Staphylococcus aureus Network Adaptive Platform (SNAP) trial (NCT05137119)."*

- **Participation Criteria**

  Please include the following sentence: *"The participant must fulfil all inclusion and exclusion criteria for the [SNAP Platform / SNAP Registry / SNAP Trial Platform or Registry] and the following inclusion and exclusion criteria to be eligible for this [domain/nested trial/prospective sub-study]:"*

9 Post-Approval & Integration (For Ratified Proposals)

The study lead, in collaboration with the SNAP Design WG and the GTMG, will be responsible for ensuring that the below items are considered in advance of their study proposal 'going live'.

9.1 EDC Integration

The SNAP Spinnaker EDC has the capacity to integrate data collection and/or keep track of participant enrolment into sub-studies/integrated domain/nested trials. Study proposals should consider whether specific data will be collected in the SNAP Spinnaker EDC or in a separate EDC, with linkage via SNAP participant unique study ID.

- All domain randomisations will be integrated into the core randomisation system, unless otherwise justified and approved.
- It is the preference that all sub-study/nested study/new domain randomisations are integrated into the central Spinnaker EDC randomisation system
- Other data points may be collected in an adjunctive EDC if preferred.

**Costs for integration into the central Spinnaker EDC will be passed along to the study leads unless otherwise agreed upon by the lead and the relevant SNAP RTMG and the SNAP GTMG. See Data Management Plan for more information on EDC and randomisation requirements.*

9.2 Operational Documentation

Below is a list of operational documents that are necessary for the development and implementation of study proposals into the SNAP Trial. Depending on the type of study proposal, the

following sections may or may not apply; please review the below points to ensure that the correct information is provided to the SNAP GTMG and RTMG for live activation of the study proposal.

Templates are available for all documents listed in Section 8; please contact the SNAP GTMG to obtain these template documents for completion.

9.2.1 CRF Data Description

If a study plans to randomise participants or **collect any additional data**, a **CRF Data Dictionary** will be required (see Data Management Plan).

If a study plans to randomise participants and/or collect additional information within the SNAP Spinnaker EDC:

- This must be discussed with the SNAP GTMG as soon as possible to confirm availability for these changes.
- The CRF data description should be completed with all datapoints and questions that are intended to be integrated into the Spinnaker platform.

10 Secondary Analyses

Data collected in the conduct of the SNAP trial and the associated registry are a rich resource for secondary analyses. The ongoing and adaptive nature of the SNAP trial means that extreme care is required before releasing any participant data from the platform database, even for small subsets or site-specific requests. To request data/samples from the SNAP Trial for secondary analysis the following documents are required for completion at the time of study completion:

- EOI for ratification by the GTSC
- Data Access Request Form – *for any SNAP Trial data requests*
- Bacterial Isolate & Data Request Form – *for any SNAP Trial isolate and isolate data requests*

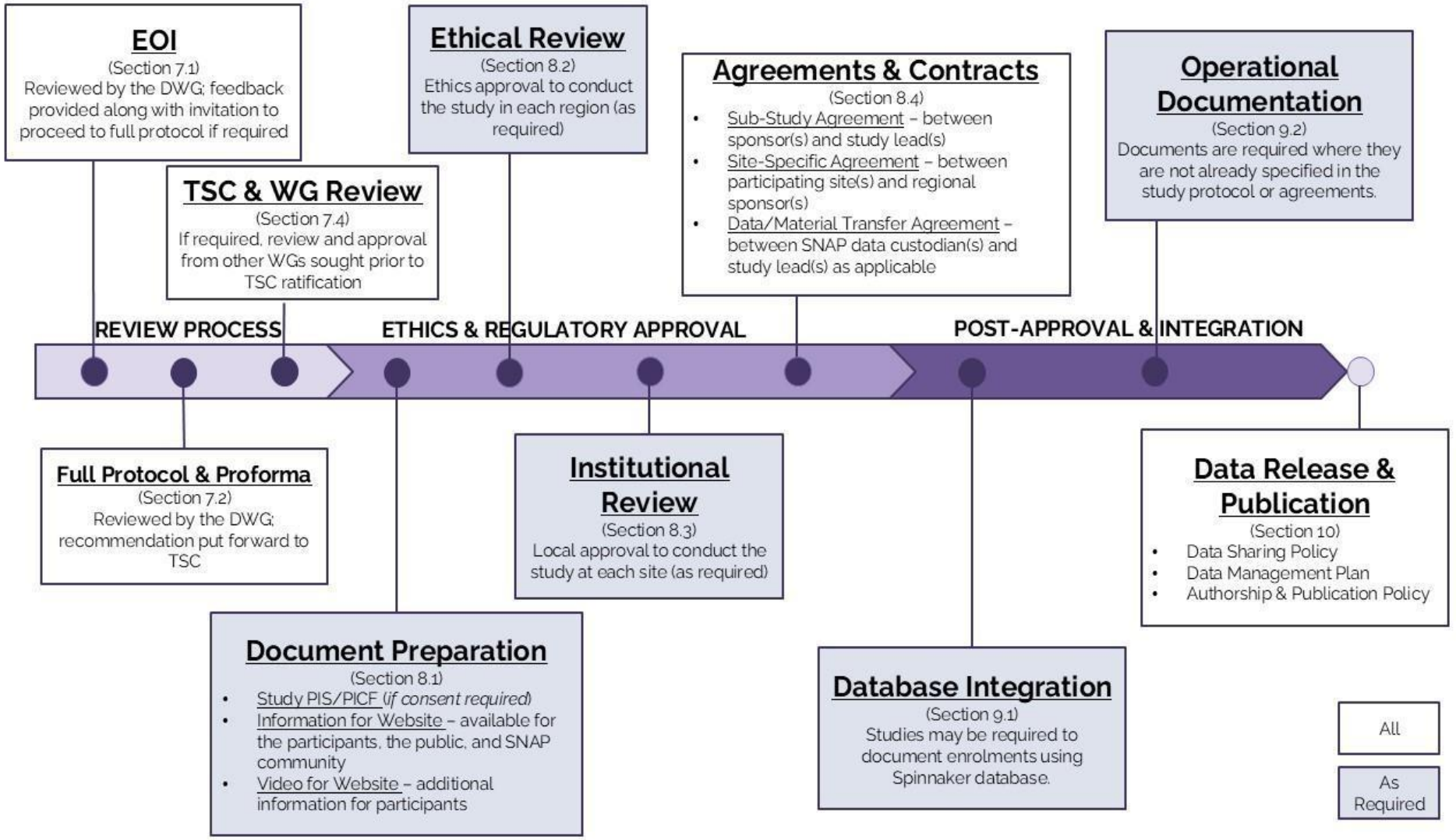
See the following documents for more information about data access and sharing, and guidance on authorship citation for SNAP studies:

- Data Sharing Policy
- Authorship and Publication Policy
- Data Management Plan
- Isolate Guidance Document

11 APPENDIX 1: RECORD OF CHANGES

VERSION NUMBER	DATE	SECTIONS AFFECTED	SUMMARY OF CHANGES	AUTHOR
1.0	15-Jul-24	-	Initial version of the document	**SG/LB**
2.0	20-Mar-26	All	Changes to study proposal review process due to the formation of the SNAP Design Working Group	**Susan Goulding**

12 APPENDIX 2: FLOWCHART OF SNAP STUDY PROPOSAL PROCESS



13 Appendix 3: Application For Co-Enrolment

Co-enrolment refers to the enrolment of an individual participant into two or more randomised clinical trials. Co-enrolment can have many advantages, and although the SNAP trial encourages and supports co-enrolment, it is important that the safety of the participants and the scientific integrity of the co-enrolling trials is considered carefully.

Clinical trials that seek to co-enrol SNAP trial participants will be subject to review and approval via the co-enrolment application process as described below. This is to ensure that potential interactions between the co-enrolling trials is considered prior to a participant being enrolled into more than one study.

All interventional clinical trials that are requesting co-enrolment with the SNAP Trial will need to complete the **SNAP Co-Enrolment Application Form**, which is available for download from the SNAP website here.

13.1 Co-Enrolment Application Review Criteria

Co-enrolment applications will be judged on the following criteria and awarded a rating of either a) major issue, b) minor issue, or c) no issue.

- **Biological interaction between interventions**
  There should be minimal or no biological interaction between the experimental interventions in the two trials. If there is a potential biological interaction, then the interventions received as part of Trial X should reflect what participants in SNAP would have been received through routine clinical care, rather than as a result of their participation in Trial X.

- **Effects on protocol compliance and intercurrent care**
  There should be minimal or no influence on SNAP protocol compliance or intercurrent care resulting from participation in Trial X.

- **Equal allocation to treatment groups**
  The treatment groups in SNAP should have equal chance of being allocated to the treatment groups in Trial X.

- **Treatment restrictions**
  Any protocol-mandated treatment restrictions in the intervention or control group of Trial X should not alter the treatment allocations in SNAP.

- **Mandated intercurrent treatments**
  Intercurrent treatment requirements in the control or intervention groups of Trial X should not substantially alter the treatments of patients in SNAP.

- **Outcome ascertainment**
  Ascertainment of outcomes in Trial X should not affect the outcomes in SNAP.

- **Clinical decision making**
  Information collected in Trial X that would not otherwise have been collected, and that is contemporaneously available, should not alter clinician decision making in any way that might affect the interventions, intercurrent care or outcomes of SNAP.

- **Adverse event procedures**
  The procedure for dealing with an adverse event in Trial X should not impact the conduct of SNAP.
- **Recruitment Cross-Over**

Trial X will be assessed for recruitment cross-over, including the likely proportion of participants enrolled with SAB and the number of patients with SAB expected to be recruited into Trial X.

- **Participant/ Site Burden**
  Trial X will be assessed for burden on the participant as well as the burden on the site team.

13.2 Co-Enrolment Application Review Process

Each study/trial that wishes to co-enrol with the SNAP trial will be required to complete a co-enrolment application form for review and approval.

- Applications for co-enrolment where the study is recruiting at SNAP recruiting sites in more than one country will be reviewed by the Global Trial Management Group (GTMG).
- Applications for co-enrolment where the study is recruiting at SNAP recruiting sites in a single country will be reviewed by that relevant Regional Trial Management Group (RTMG).

All approvals for co-enrolment will be provided to the Global Trial Steering Committee (GTSC) for noting, with the opportunity to flag concerns and challenge the approval.

13.3 Additional Working Group Review

If required, the application may be escalated for review by specific working-groups, if the RTMG/GTMG require expert opinion on any of the review criteria. These specific working groups include but are not limited to:

- **Microbiology WG**
  Applications involving isolates, or the microbiological aspects of the SNAP Trial.

- **Statistics WG**
  Applications that are believed to have an impact on the SNAP statistical model or may impact the intercurrent events.

- **Relevant Domain-Specific WG(s)**
  Applications that will have an impact on a particular domain.

- **Paediatrics and Pregnancy WG**
  Applications that intend to co-enrol paediatric or pregnant participants.

- **Health Economics WG**
  Applications that may have an impact on the collected health economic data.

- **Regional Consumer Reference Group or PPI WG**
  Applications that may increase the burden on trial participants in that region.

13.4 Co-Enrolment Application Outcomes

The outcome of co-enrolment applications will be communicated by the RTMG to the GTMG on a regular basis. The GTMG will inform the GTSC of all studies that have been approved for co-enrolment. The co-enrolment applications will be ratified by the GTSC monthly as part of the core business of the GTSC meeting.

Once an application has been ratified by the GTSC and no concerns or queries raised, the outcome will be communicated to the study requesting co-enrolment by the TMG reviewing the application (GTMG or RTMG).