

SNIP-AFRICA WORKING INSTRUCTIONS: TRIAL STEERING COMMITTEE CHARTER

The role and function of a Trial Steering Committee (TSC) are widely documented (1, 2). Since introducing TSCs within academic clinical trials, their value in providing oversight has been accepted by the scientific community as a means of ensuring the scientific integrity of a trial.

TSCs may operate in different trial environments, alongside or not a Data Monitoring Committee (DMC) or Data Safety Monitoring Board (DSMB). It is generally recommended that a TSC holds an executive role in trial oversight, considering any recommendations from the DMC/DSMB as needed. Other approaches may see the Sponsor as the sole body to hold executive power over trial conduct; however, this is discouraged as it inevitably introduces bias in the decision-making process.

Not all studies require a TSC, and it is important to reflect at the early stages of any project on the level of oversight required. A key consideration is a risk assessment to establish whether a study or trial can be considered lower risk.

In general, most observational studies will fall into this group (a Trial Within a Cohort Study or TWICS could be an exception). A trial may be lower risk if the intervention is low-risk or used widely in regular practice, the participants are not considered to be a vulnerable group, and the risk status is expected to remain stable. Furthermore, a trial management group or team experienced in trial conduct and management is necessary to forgo a TSC in lower risk trials.

The default for any interventional study on the SNIP-AFRICA platform, including studies that collect samples beyond what is planned as part of routine care, should be to establish a TSC to provide oversight. Use of “umbrella” TSCs” for multiple related studies or trials may be an efficient approach and works well for low-risk studies and trials.

SNIP-AFRICA PLATFORM

The SNIP-AFRICA platform includes three complementary domains that operate independently within the platform.

Work Package 2: Clinical and microbiological surveillance

The aims of WP2 are:

- To establish a surveillance platform for neonatal sepsis and a perpetual platform for early detection, evaluation and response to outbreaks or shifts in antimicrobial resistance in SSA sites.
- To create a streamlined, translatable data capture and sampling approach across a range of health facilities which is appropriate in the context of the SNIP-AFRICA architecture.
- To develop a real time data dashboard to drive quality improvement at the level of contributing sites based on rates and trends in neonatal sepsis, blood culture findings and outcomes.
- To identify changes in resistant bacterial prevalence, including to trial drugs, over time and to relate neonatal blood culture isolates to faecal carriage, the hospital environment and antimicrobial usage.

Work Package 4: Pharmacokinetics for Adaptive Platform Trial

The aims of WP4 include:

- To *develop the PK domain-specific appendix* to the core protocol for neonatal and infant antimicrobial dose finding or confirmation.
- To *develop domain-specific electronic case record forms (eCRFs)* to capture data using a secure online open-source data registry to facilitate standardised clinical trial data collection.
- To *develop a domain-specific pharmacometrics analysis plan* to facilitate timely reporting of results for dose finding or confirmation.
- To enable the *conduct of relevant PK studies* within the SNIP-AFRICA platform.

Work Package 5: Complex Adaptive Drug Regimen Trial

The objectives of Work Package 5 are:

- To co-develop and implement country and site-specific drug-regimen appendices to investigate relevant empiric regimens for neonatal sepsis in different African neonatal units within the platform trial.
- To conduct an innovative adaptive platform trial using combined Personalised RAndomised Controlled Trial (PRACTical) and Sequential Multiple Assignment Randomised Trial (SMART) designs.
- To develop a blueprint for domain-specific eCRFs and web-enabled data collection in collaboration with WP2 and WP4.
- To collaborate with WP2 and WP4 to develop domain-specific adaptations responding to emerging project, trial, and other global data.

ADAPTING THE CHARTER TEMPLATE

This document provides working instructions for the development of the Trial Steering Committees Charter for platform domains within the SNIP-AFRICA project.

This template should form the basis for each individual study's or trial's charter, but its content should be revised and adapted as necessary.

The Charter should be completed before (or early into) the trial and the content should be agreed with the TSC members. Separate agreements will be signed by independent and non-independent members. All attending observers may be asked to sign a confidentiality agreement and declare any potential competing interests at their first meeting or on each occasion where their potential competing interests have changed.

All highlighted sections should be updated and replaced where relevant or deleted otherwise (e.g. guidance notes); revisions are, of course, permitted to the standard non-highlighted text where appropriate but please bring these changes to the special attention of the SOP Committee as such changes may be incorporated into the next updated of this template Charter. All embedded comments should be removed.

SPONSORSHIP

The SNIP-AFRICA platform includes the cooperation of several legal Sponsors to operate each domain. A multi-sponsor approach is being used within SNIP-AFRICA, with WP3 offering a governance framework for the platform which does not preclude the presence of multiple Sponsors.

FUNDING

When adapting the TSC Charter, please ensure that all funder's requirements are met, and consideration is paid to ensure this oversight body can fulfil its responsibilities in line with its Charter.

References

1. Conroy EJ, Arch B, Harman NL, Lane JA, Lewis SC, Norrie J, et al. A cohort examination to establish reporting of the remit and function of Trial Steering Committees in randomised controlled trials. *Trials*. 2017;18(1):590.
2. Harman NL, Conroy EJ, Lewis SC, Murray G, Norrie J, Sydes MR, et al. Exploring the role and function of trial steering committees: results of an expert panel meeting. *Trials*. 2015;16:597.