

1 Purpose and overview:

This SOP¹ provides guidance in the monitoring and reporting of deviations from the Institutional Review Board-approved LAKANA protocol.

This SOP refers to Data Collection Form (DCF) DCF014, and DCF15.

2 Applicability to and responsibilities of various staff members

Principal Investigators (PIs) and study team (e.g., coordinators as well as study statistician, monitors, data managers, researchers) are all responsible for detecting and reporting deviations from the approved protocol. The PIs will assist the study sites with handling deviations.

3 Required materials

Item	Number	Specification
Tablet or Table computer with Tangerine application installed	<i>As needed.</i>	The following questionnaires will be loaded: DCF014, DCF15.

4 Definitions and general instructions

4.1 Definitions

4.1.1 Protocol deviation: An unplanned excursion from the Institutional Review Board-approved protocol not intended as a systematic change.

4.1.1.1 Only deviations due to the investigation team will be considered protocol deviations.

4.1.1.2 Deviations due to study participants (e.g. participant failing to show up at a health facility visit) are acceptable and will not be reported as protocol deviations.

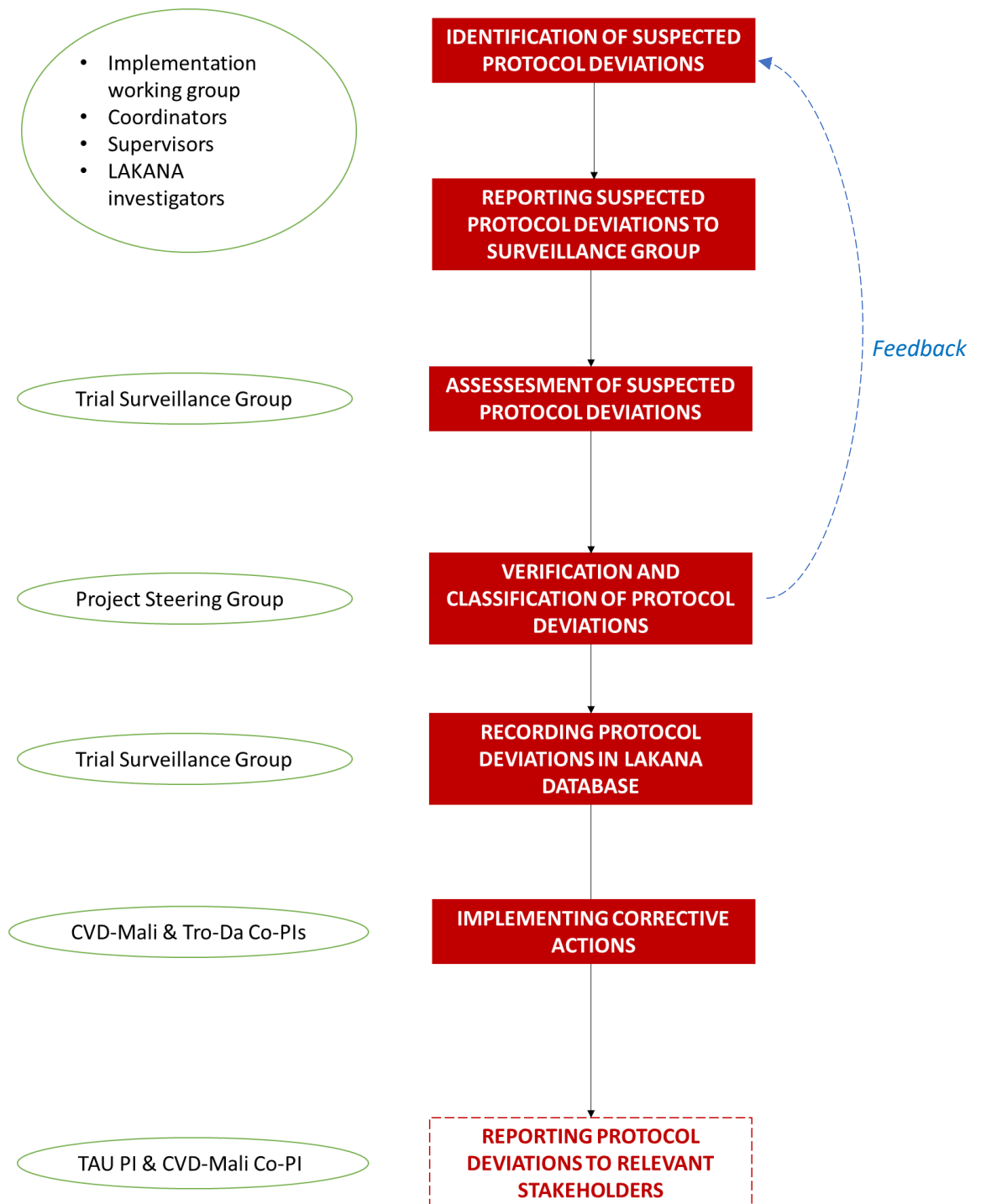
4.1.2 Site-level protocol deviation: a situation where the protocol deviation is not tied to a specific individual subject but has impact on all or multiple subjects enrolled at that site. For example, a temperature excursion occurring at a given site will have impact on all subjects that are treated with the affected drugs - this is a site level protocol deviation.

¹ Abbreviations: SOP = standard operating procedure, DCF = data collection form, DSMB = Data safety monitoring board, IRB = Institutional review board, LAKANA = Large-scale assessment of the key health-promoting activities of two new mass drug administration regimens with azithromycin, MDA = mass drug administration, PI = Principal Investigator.

- 4.1.3 Individual-level protocol deviation: a situation where the protocol deviation is tied to a specific individual subject. For example, an infant who is given an incorrect study drug dose.
- 4.1.4 LAKANA Coordinator: A CVD-Mali LAKANA investigator who monitors the trial activities (ranging from management of study drugs at storage facilities to data collection and MDAs in villages etc.) for adherence to the study procedures.
- 4.1.5 LAKANA Supervisor: A CVD-Mali LAKANA staff member responsible for coordinating data collection teams' activities. S/he is under the supervision of the LAKANA coordinator.
- 4.1.6 LAKANA Trial Surveillance Group: a team composed of LAKANA investigators designated by the IWG and responsible for activities related to protocol deviations and SAE monitoring (assessment, and reporting activities).

4.2 General instructions

4.2.1 The flowchart below describes the main steps regarding the identification and reporting of protocol deviations. The detailed instructions are described in *Section 5 Step-by-step procedures*.



5 Step-by-step procedures

5.1 Identification and reporting of suspected protocol deviations

5.1.1 Suspected deviations in the LAKANA trial will be reported to the Trial Surveillance Group by e-mail at this address: lakana.tsg@lists.tuni.fi .

- The type of information to provide to the surveillance group when reporting a deviation is documented in [Appendix 1](#).

5.1.2 All LAKANA staff members collecting data and/or study samples will immediately notify their supervisors (as defined in section 4.1.5) if they suspect that that they have made a protocol deviation.

- If they suspect that their colleagues have made a deviation, they will encourage them to report the suspected deviations to a LAKANA supervisor.

5.1.3 The LAKANA supervisors will monitor data collectors' and nurses' activities and report by e-mail (or any other available communication channel) and immediately upon awareness, any unapproved changes or divergence from the study procedures to the LAKANA Coordinator.

5.1.4 The LAKANA coordinator will regularly liaise with the field team including LAKANA pharmacist and drug managers, and supervisors. The coordinator will report any detected deviations by e-mail to the surveillance group (at maximum within 2 days of becoming aware of a deviation).

5.1.5 On a weekly basis and upon availability of data exports, a TAU statistician produces descriptive statistics and makes them available to all LAKANA investigators through LAKANA repository. The surveillance group will review the descriptives as they become available and identify issues to be further assessed. Assessment will be done as described in 5.2.1.1.

NB: All LAKANA investigators have access to TAU repository and hence are encouraged to review the data as well and report any suspected deviations to the surveillance group.

5.1.6 On a weekly basis and upon availability of data exports, a TAU statistician produces a list of queries. This list is to be sent to the CVD-Mali team for data correction purposes. As protocol deviations might also be detected from the list of queries, the surveillance group will review the list of queries as they become available and identify issues to be further assessed.

5.1.7 The implementation working group, constituted of researchers from CVD-Mali, TroDa, and TAU, meets on weekly basis to review trial activities. During these meetings, the group will discuss any issues that have occurred during the preceding week and determine what events should be further assessed by the surveillance group.

5.2 Protocol deviations assessment, verification and recording

5.2.1 Upon receiving a notification of a suspected protocol deviation, the surveillance group will arrange a meeting and review the case(s) for pre-confirmation of the deviation(s). The group will fill in the protocol deviation form(s) (**in Microsoft Word**). The forms are available at LAKANA repository. See [Appendix 2](#) for details on the form content and instructions for completion.

5.2.1.1 The surveillance group will assess whether a deviation meets IRB reporting requirements and document it in the protocol deviation form. Deviations from the protocol that cause or could cause harms to the trial subjects, or affect their rights, or significantly affect the conduct of the trial will be reported to these instances. The categories of deviation to be reported to the IRB, DSMB, and Funder are:

- 1- Inadequate informed consent
- 2- Use of expired medication or medication not approved for use (reasons may include e.g. temperature excursion, damage to the products).
- 3- Other deviation that may have violated the participant's rights or place her / him at an increased risk of adverse consequences

5.2.1.2 Only deviations falling under category 2 will be reported to Pfizer.

5.2.2 Upon completion, the surveillance group will send, by e-mail and at lakana.psg@lists.tuni.fi, the protocol deviation form(s) to the PSG for review.

5.2.3 The PSG will send back by e-mail the approved version of the form(s) or confirmation to the surveillance group who will then proceed with documenting the data in the electronic data capture system used in the LAKANA trial.

5.2.3.1 The PSG will provide a feedback on the suspected deviations that were reported to the concerned LAKANA investigators. The feedback can be provided to the concerned investigators through the Implementation Working Group.

5.3 Implementing corrective actions and reporting to stakeholders

5.3.1 If applicable, the PSG will report the protocol deviations to the designated parties:

5.3.1.1 TAU PI will inform the DSMB, the Funder, and Pfizer.

5.3.1.2 CVD-Mali co-PI will inform the Malian IRB and other Malian authorities, if necessary.

5.3.2 TroDa and CVD-Mali co-PIs will ensure the immediate implementation of all corrective measures decided by the PSG to avoid recurrences of the concerned deviations.

5.3.3 The protocol deviation summary/listing will be filed in the TAU Trial Master File and the CVD-Mali site will archive the summary/listing concerning the site in the site study documentation folder.

6 Occupational Safety Issues

None.

7 Quality Assurance / Quality Control

The PSG will ensure the accuracy, and timeliness of the data reported to the IRB, DSMB, Funder, and Pfizer.

8 Appendices and other related documents

[Appendix 1](#): Form for reporting suspected deviations to the surveillance group

[Appendix 2](#): Instructions for filling in protocol deviation forms

DCF14: Individual-level protocol deviation form.

DCF15: Site-level protocol deviation form.

9 Version history, authors, and approvals

Version (date)	Edits to the SOP text (author)
Version 1.0 (2021-06-22)	Authored by Laura Adubra in consultation with Per Ashorn, Riku Elovainio, Yuemei Fan and the IWG. Approved by the LAKANA PSG.

Appendix 1: Form for reporting suspected deviations to the surveillance group (lakana.tsg@lists.tuni.fi)

Section 1: General Information	
1- Name of LAKANA investigator reporting the suspected deviation	
2- Date of reporting	
3- Site where the suspected deviation occurred:	<input type="checkbox"/> Bamako Pharmacy <input type="checkbox"/> Kita Pharmacy <input type="checkbox"/> Bamako Lab <input type="checkbox"/> Kita Lab <input type="checkbox"/> CSCom <input type="checkbox"/> Village <input type="checkbox"/> NA (<i>if deviations identified through data descriptives, go to section 2, If deviation identified through queries, go to section 3</i>)
4- If village, specify name of village	
5- If CSCom, specify name of CSCom	
6- Description of the event (including how and why the deviation occurred) Specify participant IDs when applicable (Compound, household, Child ID) <i>For study drug related deviations, specify identifiers (letter code, bottle number) of affected medication</i> <i>For laboratory related deviations, specify IDs of affected specimens</i>	
7- Immediate corrective actions taken (if any)	
Section 2. Suspected deviation identified through data descriptives	
8- Type of data descriptives where the issue is located	<input type="checkbox"/> Main Cumulative <input type="checkbox"/> Main Last week <input type="checkbox"/> AMR Cumulative <input type="checkbox"/> AMR Last week
9- If applicable, specify Data collection form where the issue is located	
10- If applicable, specify question and variable name	
11- Description of the issue	
Section 3: Suspected Deviation identified through data queries	
1- Record ID	
2- Visit Number	
3- Data collector name	
4- Data collection form	
5- Question number	
6- Variable	
7- Suspected issue	

Appendix 2: Instructions for filling in protocol deviations

All protocol deviation forms submitted will include the following information:

- **Supervisor Identifier:** last name and first name of the person filling in the form.
- **Child ID** (only for DCF014): the individual subject ID affected by the deviation.
- **Date of reporting:** Date when the protocol deviation form is completed.
- **Protocol deviation date:** Date when the protocol deviation occurred.
- **Protocol deviation start date** (only for DCF015).
- **Protocol deviation end date** (only for DCF015).
- **Deviation category:** in LAKANA, the list of deviation categories includes
 - **Inadequate process for obtaining consent.**
 - Other deviation in the provision of information about the trial
 - Incorrect enrolment (e.g. participant enrolled but does not meet protocol eligibility criteria; participant met withdrawal criteria during the study but was not withdrawn)
 - Deviation in the implementation of household visits (e.g. wrong date, missed visit due to the investigation team).
 - A delay between two MDAs will be flagged as a protocol deviation using a +/- 4-week window. I.e. for a given village, a follow up MDA that starts 4 weeks before or 4 weeks after (from start to start dates) the 3 months interval will be considered a deviation.
 - **Use of expired medication or medication not approved for use (reasons may include e.g. temperature excursion, damage to the products).**
 - Other deviation in the storage, transport, or provision of study drug
 - Incorrect measurement of trial outcomes
 - Data entry or management errors (e.g. errors in transmission, wrong coding)
 - Deviation in laboratory assessments/procedures (e.g. wrong sample collection, problems in cold chain, mistakes in testing)
 - Error in Serious Adverse Event Reporting (e.g. not reporting an SAE within required timeline)
 - **Other deviation that may have violated the participant's rights or place her / him at an increased risk of adverse consequences.**
 - Other (to be specified in the form)
- **Description of the deviation:** For study drug related deviations, IDs of affected medication will be documented. For laboratory deviations, IDs of affected specimens will be documented.
- **Steps taken to resolve or avoid recurrence of the deviation.**
- **Confirmation of whether the deviation result in an adverse or serious adverse event.**
- **Confirmation of whether the affected subject will continue to participate in the study.**