

Standard Operating Procedures for the LAKANA trial  
**SOP Subvisit-01: Conducting Sub-study Visit 01.**  
 Version 2.0 (2021-04-20)

### 1. Purpose and overview:

This SOP<sup>1</sup> provides step-by-step instructions on how to conduct the Sub-study Visit 01 (MDA #1S<sup>2</sup>) for the LAKANA secondary outcome sample formed from villages around the four selected health centers close to the city of Kita.

This SOP refers to SOPs Visit 01, Prep-02, Pharm-01, Proc-01, Proc-04, Proc-05, Proc-06, Proc-11, Safety-01, and Data Collection Form (DCF) DCF01 (a,b,c,d,e,f), DCF02, DCF02a, DCF02b, DCF03, DCF04, DCF05, DCF08, and DCF13/13a.

### 2. Applicability to and responsibilities of various staff members

Staff member	Responsibility
District Supervisor	<ul style="list-style-type: none"> <li>- Plans date of entry in a village, in consultation with study coordinator.</li> <li>- Prepares study drugs and data collector's material to be dispatched from Kita to CSCoM.</li> </ul>
Lab technician	<ul style="list-style-type: none"> <li>- Prepares sample collection bags in which swabs, tubes with medium and labels for rectal and nasopharyngeal swab sample collection are included in Bamako, prepare also other collection material to be dispatched from Bamako to Kita and to CSCoM.</li> <li>- Handles samples in the Kita/Bamako lab.</li> </ul>
Field Supervisor	<ul style="list-style-type: none"> <li>- Agrees on date of entry and equipment rental with village chief.</li> <li>- Works with nurse to transport study material from Kita to CSCoM and store.</li> <li>- Packs data collectors' rucksacks.</li> <li>- With study nurse, manages the disposal of study waste.</li> </ul>
Study nurse	<ul style="list-style-type: none"> <li>- Packs sample collection material at CSCoM and arranges transport to village.</li> <li>- Coordinates the setting up of the pop-up facility in village.</li> <li>- Completes DCF13 and DCF02b in tablet computer or in paper form 13a-AMR (Appendix 1) and DCF02b (Appendix 3).</li> <li>- Completes sample logbook (Appendix 2).</li> <li>- Collects biological samples from 4-14 mo. and 49-59 mo. old children and ensures samples are correctly labelled, transported to and deposited in Kita lab.</li> </ul>

<sup>1</sup> Abbreviations: SOP = standard operating procedure, DCF = data collection form, AMR = antimicrobial resistance, CSCoM = Centre de Santé Communautaire, LAKANA = Large-scale assessment of the key health-promoting activities of two new mass drug administration regimens with azithromycin, MDA = mass drug administration, NPS = nasopharyngeal swab.

<sup>2</sup> MDA #1S indicates MDA round 1 for villages included in the Sub-study.

	- Provides study drug to 4-11 mo. old infants after sample is collected.
Data collector	- Finds the compound/households and requests permission to proceed. - Operates tablet computer - completes DCF01 (a,b,c,d,e),02(a),03,04,05,08. - Provides study drug to 1-3 mo. old infants. - Prepares study drug for 4-11 mo. old infants.
Relais	- Helps data collector to identify compounds and households. - Guides of 4-14 mo. and 49-59 mo. old children and their caregivers to pop-up facility. - Assists data collector in study drug administration.
Driver/ messenger	- Ensures the transport of nurse and sample collection material between CSCom and village. - Assists nurse in setting up pop-up facility. - Ensures the safe transport of sample collected in village to Kita lab.

**3. Required materials** (only show specifically for Sub-study visit 1, for material related to MDA, refer to SOP Visit-01)

Item	Number	Specification
Identification Sticker for <b>1-11</b> mo. old infants	2 identical stickers per child	2 identical stickers (with QR code/ID): <ul style="list-style-type: none"> <li>• One sticker to be affixed on <b>child health card</b>.</li> <li>• Second sticker to be affixed on the data collector's paper register.</li> </ul>
Identification Sticker for <b>12-14</b> mo. and <b>49-59</b> mo. old children	2 identical stickers per child	2 identical stickers (with QR code/ID) to be affixed on <b>LAKANA card</b> .
LAKANA card - <b>YELLOW</b>	<i>As required</i>	Card for <b>4-5</b> mo. old infants.
LAKANA card – <b>BLUE</b>	<i>As required</i>	Card for <b>6-8</b> mo. old infants.
LAKANA card - <b>GREEN</b>	<i>As required</i>	Card for <b>9-11</b> mo. old infants.
LAKANA card – <b>PINK</b>	<i>As required</i>	Card for <b>12-14</b> mo. old children <b>Card where the child sticker will be affixed.</b>
LAKANA card - <b>VIOLET</b>	<i>As required</i>	Card for <b>49-59</b> mo. old children <b>Card where the child sticker will be affixed.</b>

<b>Item</b>	<b>Number</b>	<b>Specification</b>
Tent	1	A pop-up medical tent to be set up in the village.
Table	1	Rent from village.
Chairs	3	Rent from village.
Clinical waste bin	1	To be kept at the pop-up facility.
Nurse's Tablet computer	1	The following questionnaire will be loaded: DCF02b, DCF13
DCF13a, hard copy Appendix 1	<i>As required</i>	The paper version DCF13a needs to be filled by study nurse for sample collection if Tablet computer or electronic DCF13 are not functional
Sample logbook, hard copy Appendix 2	<i>As required</i>	The study nurse ALWAYS fill the sample logbook for each sample collected.
DCF02b, hard copy Appendix 3	<i>As required</i>	The paper version DCF02b needs to be filled by study nurse after sample collection if Tablet computer or electronic DCF02b are not functional
Sample bag	1 sample bag/participant <i>Number required to meet the daily target</i>	Each sample bag includes two smaller zip bags. The "Rectal" one includes 3 flocked swabs (Copan swab with 30mm breakpoint - 520CS01), one 2mL tube with 1mL Cary Blair media, one 2mL tube with 1mL DESS, and one empty 2mL tube. The "NP" one includes 1 nasopharyngeal flocked swab (Copan swab with 100mm breakpoint - 503CS01), one 2mL tube with 1mL STGG media. Each tube with barcode label sticker on it.
Extra bag of Flocked swabs (both rectal swabs and nasopharyngeal swabs)	<i>Extra number in case needed</i>	Each bag includes 20 flocked rectal swabs (labelled with "extra rectal swabs) or 20 flocked nasopharyngeal swabs (labelled with "extra NP swabs). To protect from the contamination if the swab in the sample bag touch other surface or sample is not collected properly and need to be collected again
Disposable gloves	2 pairs/participant <i>Number required to meet the daily target</i>	

Item	Number	Specification
Baby wipe	1 wipe/participant <i>Number required to meet the daily target</i>	To wipe the child's bottom prior to rectal swab sample collection.
Cooler box	1	Electric cooler box (12v).
Min/max-temperature monitors	1/cooler box	For determining whether temperature excursion occurred and for how long (e.g. as MyM Instruments Tecnico Product Number HTC-2 or Fisher Scientific <sup>TM</sup> Traceable Thermometer <u>14-648-26</u> )
Paper towel	<i>Number required to meet the daily target</i>	
Biohazard waste bag	1	
70% ethanol	1	500 ml
Surgical mask/ N-95 mask	<i>Number required to meet the daily target</i>	
Goggles or face shield	1	
Refrigerator	1/CSCoM	To store and maintain transport media at appropriate temperature (2-8°C) and prepare/store ice packs to be used for maintaining cooler boxes.
Ziplock bag	<i>As required</i>	To transport syringes from household to the pop-up facility

#### 4. Definitions and general instructions

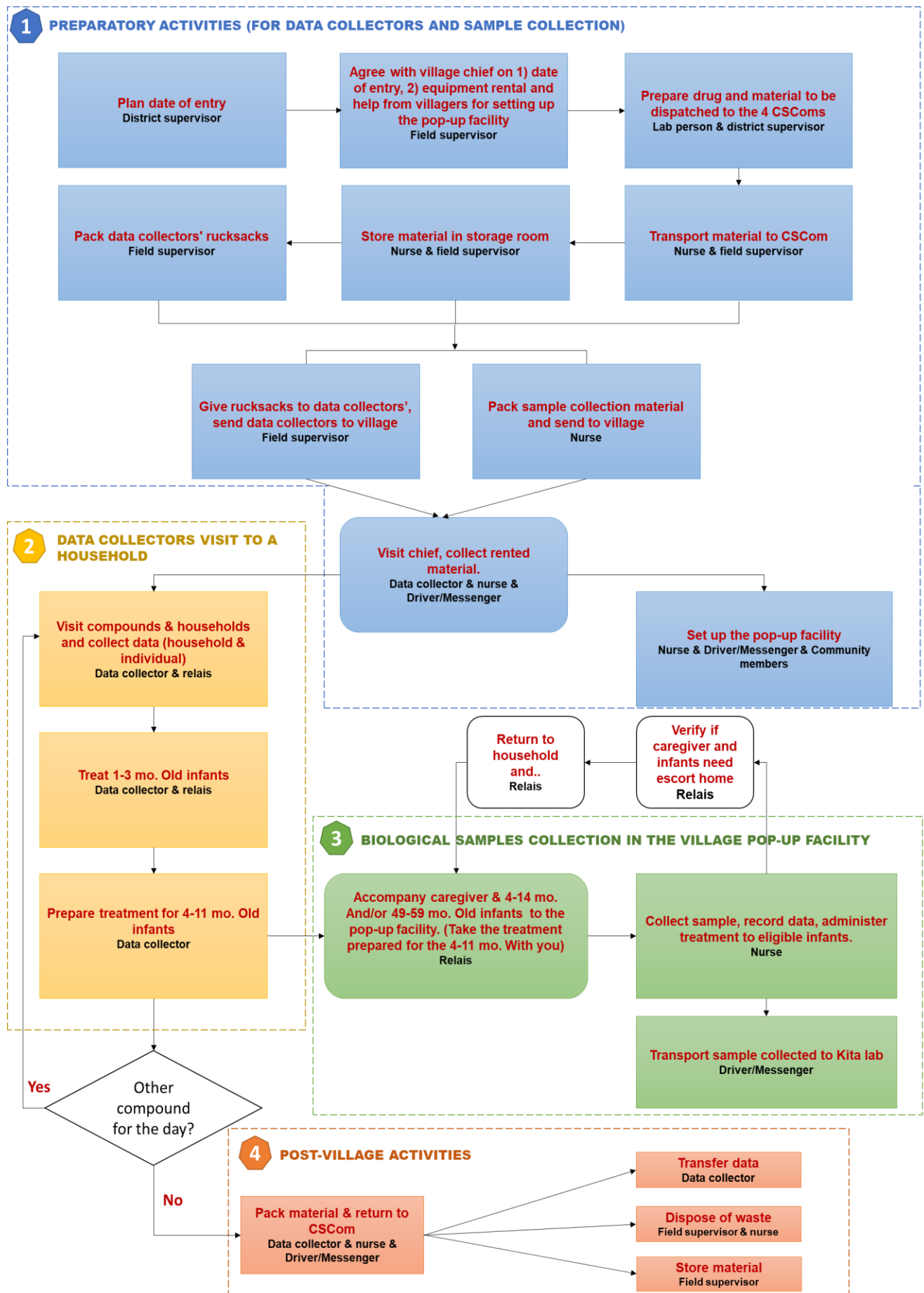
##### 4.1. Definitions

- 4.1.1.** District supervisor: a LAKANA staff member coordinating trial activity at the district level. The district supervisor reports primarily to the study coordinator and is stationed in the district office.
- 4.1.2.** Lab technician: a LAKANA staff member based in Bamako or Kita (Bamako or Kita lab), and responsible for preparing sample collection bags and material for study nurse and handling specimens brought from villages.
- 4.1.3.** Field supervisor: a LAKANA staff member responsible for coordinating data collection teams' activities. S/he is under the supervision of the District supervisor.
- 4.1.4.** Relais Communautaire: a volunteer chosen by the community who serves as a bridge between professional health staff and the villagers.

- 4.1.5.** Study nurse: a LAKANA staff member responsible for AMR and mechanistic sub-study data and sample collection.
- 4.1.6.** Data collector: a LAKANA staff member collecting data at the compound, household, and individual level.
- 4.1.7.** Eligible infant: an infant aged between 1 and 11 months (age 29-364 days) and weighing at least 3.0 kilograms at the time of study drug provision, and for whom there is no record of allergy to macrolides.
- 4.1.8.** Eligible child for Sub-study: a child aged between 4-14 or 49-59 mo. living in a household that consented to participate in the LAKANA trial. Consent for participation in the Sub-study will be requested from head of each household including all children in the household.
- 4.1.9.** Caregiver: a person responsible for looking after a child. The caregiver is responsible for providing permission for study drug administration to eligible infants.
- 4.1.10.** Pop-up facility: refers to a temporary clinical facility (a village central place or a tent equipped with appropriate sample collection material) that the LAKANA team will set up in a village for sample collection purposes.

## **4.2. General instructions**

- 4.2.1.** The four main processes – 1) Preparatory activities (for data collectors and sample collection), 2) Data collectors visit to a household, 3) Biological samples collection in a central site in the village, and 4) Post-village activities - for conducting sub-study visit 01 are illustrated in the figure below and detailed instructions for each phase are provided in Section 5 Step-by-step procedures.



## 5. Step-by-step procedures

### 5.1. Plan date of entry:

- 5.1.1. The district supervisor will review and edit the individual village dates of entry if needed (*Refer to SOP Prep-02*). He will confirm the dates to the field supervisor.

### 5.2. Agree with village chief:

- 5.2.1. Prior to entry in a village (~1 week), the field supervisor will agree with the chief of the village on the date of entry. At this occasion, the field supervisor will discuss the rental of some material (1 table + 3 chairs) and help from the community to set-up a pop-up facility for sample collection in the village.

### 5.3. Prepare material for a CSCoM:

- 5.3.1. At the Bamako lab (~1 week prior to date of entry in village), the lab team will prepare the sample collection bags (*Refer to SOP Pro-04*) and material to be dispatched to the Kita district office and kept at 2-8°C.

- 5.3.1.1. The transport media needs to be aliquoted to 2 ml screw cap tubes before a village MDA. The laboratory technician will aliquot 1 ml Cary Blair transport media, 1 ml DESS and 1 ml STGG to 2 ml screw cap tubes and affix each tube with pre-printed unique barcode label sticker. S/he will prepare enough tubes in advance, store them (2-8°C) and test the medium 1 week before packing to make sure the medium is in good condition and not contaminated (*Refer to SOP Pro-04, Appendix 1-3*).

- 5.3.2. Trial drugs are stored in Kita. The district supervisor, in consultation with the drug manager, will pack the drugs (making sure the right study drug for each village is selected) to be transported to the CSCoM. *Refer to SOP Pharm-01 for details on drug management.*

### 5.4. Transport material from Kita to CSCoM and store:

- 5.4.1. The day before entry in a village, the nurse and field supervisor will pick up the material prepared and arrange the transportation to the CSCoM.

- 5.4.1.1. The quantity of study drugs and sample collection bags and material to be picked up will cover at least one week of activities per village.

- 5.4.1.2. During transportation, the sample collection bags will be kept at 2-8°C.

- 5.4.2. The nurse and field supervisor will store the material in the LAKANA storage room at the CSCoM.

- 5.4.2.1. The storage room is equipped with a refrigerator where the nurse will store the sample bags at 2-8°C.

- When going to the village, the nurse will keep the sample bags at 2-8°C in the electric cooler box.

- 5.4.2.2. The drugs will be kept in the storage room for a week or less therefore there will be no need for cold chain. The storage room will be however equipped

with a thermometer to signal very important rise of temperature (*refer to SOP Pharm 01*).

- 5.4.3.** The field supervisor will contact the data collectors assigned to the village and set an appointment at the CSCom on the morning of the date of entry in the village.

**5.5. Entry in a village:**

- 5.5.1.** On the morning of the date of entry in a village, the field supervisor will prepare and distribute the rucksacks to the data collection team (*Refer to SOP Visit-01 for details*). The study nurse will pack the sample collection material needed for the day.
- 5.5.2.** The whole team will move together to the village. The data collector has his/her own transportation and a LAKANA driver/messenger will transport the nurse and the sample collection material.
- 5.5.3.** The field supervisor will visit the data and sample collection team to provide technical support, when needed. When on-site visits are not possible, the field supervisor will rely on regular phone calls.
- 5.5.4.** Upon arrival in a village and only on the first day, the LAKANA team will visit and greet the chief of the village. With the instructions from the chief, they will find the village central place for setting up the pop-up facility where the participants' samples will be taken. The rented materials (1 table and 3 chairs) will be provided. The LAKANA team will request assistance in setting up the pop-up facility.
- 5.5.5.** The data collector accompanied by two Relais will start visiting compound/households.
- 5.5.6.** The nurse, the driver/messenger and the community members will set-up the pop-up facility.

**5.6. Data collection in household and treatment of 1-3 mo. old infants:**

- 5.6.1.** The data collector will follow the procedure described in *SOP-Visit 01* for conducting the visit with some exceptions:
- 5.6.1.1. Consent for participation in Sub-study: The data collector will seek consent to participate in Sub-study from head of each household including all children in the household. (*see definition of eligible child in 4.1.8*).
- 5.6.1.2. Data collection forms: In the Sub-study Visit 01, one additional form will be used in the household: DCF08 (for 4-14 mo. old children) administered by the data collector to collect morbidity data. In the household, the data collector will collect information in the following order:
- Form 1a Compound Enumeration
  - Form 1b Household Enumeration
  - Form 1f Household Consent



- Form 1c Adult Enumeration
- Form 1d Child Enumeration (for all children)
- Form 2 Child Treatment (for all 1-11 mo. old infants)
  - NB: for **4-11** mo. old infants, the data collector will select the answer “**Study Nurse**” at the question ““Who is planned to give medication””.
- Form 3 Immunization (for all 1-14 mo. old infants)
- Form 8 Morbidity (for all 4-14 mo. old infants)
- Form 4 Assets
- Form 5 WASH

5.6.1.3.LAKANA cards: The data collector will issue colored LAKANA cards to children eligible for Sub-study. The purpose of these colored cards is to differentiate children’s age-groups so that at the pop-up facility the nurse can identify what sample to collect according to the child’s age. In the household, the data collector will give different colored card to children for whom there is a household consent to participate in Sub-study:

- **Yellow** card to **4-5** mo. old infants
- **Blue** card to **6-8** mo. old infants
- **Green** card to **9-11** mo. old infants
- **Pink** card to **12-14** mo. old children
- **Violet** card to **49-59** mo. old children

5.6.1.4.ID stickers:

- For **1-11 mo.** old infants, the procedure for issuing ID stickers is the same as in the main study i.e. for each 1-11 mo. old infant the data collector will affix an ID sticker on the **child health card** (*See SOP Visit 01, Appendix 5*). The data collector will instruct the caregiver with **4-11 mo.** old infants to bring **BOTH** the child health card (that has the sticker) and the LAKANA colored card when visiting the pop-up health facility for sample collection.
- For **12-14** and **49-59** mo. old children the data collector will affix the ID stickers on the **LAKANA colored card**. The data collector will instruct the caregiver to bring the colored card (that has the stickers) when visiting the pop-up health facility for sample collection.
- When there are more children in the same age range in some households, the data collector will add the age range and the name of each child to the colored card in addition to the child ID sticker.

5.6.1.5.Treatment:

- The data collector will prepare and administer study drug **ONLY** to eligible **1-3 mo. old infants** for whom there is a caregiver permission for treatment. *Refer to SOP-Proc 1 for procedure on study drug Administration.*
- For **4-11 mo. old infants**, if permission for treatment is given, the data collector will weigh and complete information on form DCF02. Completing the form will allow to determine study drug dose to be prepared for the infants. The data collector will prepare the study drug, **but s/he will NOT administer the drug to infants**. The data collector will place the syringe containing the study drug in a zip lock bag and give it to the Relais or the caregiver.

**5.6.2.** For **all 4-14-mo. and 49-59 mo. old children** (for whom there is a household consent for participating in the sub-study), the Relais will accompany the caregiver and the children to the pop-up facility for sample collection. The Relais will make sure the caregiver of each child has the LAKANA colored card, health card (if applicable) and syringe (if applicable).

**5.6.3.** The data collector will continue with his activities in the households/compound (repeat step 5.6)

- NB: There are two Relais in the data collection team so that there is always a Relais available to accompany a caregiver to the pop-up facility.

## **5.7. Data and Sample collection at pop-up health facility and treatment of 4-11 mo. old infants.**

**5.7.1.** Every time a Relais will arrive at the pop-up facility with an eligible child for sample collection:

5.7.1.1. The nurse will open a new record (DCF13) on his/her tablet and start entering ID data.

- If the child age is between 4-11 mo., the ID will be found on the health card
- If the child age is between 12-14 or 49-59 mo., the ID will be found on the LAKANA colored card.
- NB: If entering the child ID information is not working, fill in the DCF13a-AMR paper form (Appendix 1). Study nurse will **ONLY** fill sample collection form DCF13a-AMR paper version **WHEN** the electronic DCF13 in the TABLET is **NOT** working.

5.7.1.2. Based on the LAKANA colored card the child has, the nurse will select the corresponding age group on the tablet. By doing so, the data collection system will indicate the required samples to collect. The nurse will explain the sample collection procedure and give instructions to the caregiver.

5.7.1.3. The nurse will collect the samples: rectal swabs and nasopharyngeal swab samples at Visit 01 (*Refer to SOP\_Proc-05 and Proc-06*) and record information on DCF13.

- The nurse will ensure the specimen storage in the appropriate temperature and condition in the cooler box. S/he will ensure that samples are correctly recorded and connected to the child ID – scan the barcode on the sample tubes to the tablet.

Note: When there is no barcode label for the sample vial, the study nurse will handwrite the following information on the collected sample vial.

**LAKANA-AMR, MDA1 (or short version LA1)**

**Child ID (MUST be clear and recognizable)**

**Child age (age group in months)**

**Date of sample collection**

5.7.1.4. After samples are collected and information entered in DCF13, the nurse will fill the sample logbook for each sample collected (Appendix 2). The nurse will also keep the LAKANA colored card in a dedicated box. S/he will not give back the colored card to the caregiver.

5.7.1.5. The nurse will treat the eligible **4-11** mo. old infant (the syringe with study drug was pre-prepared and brought by the Relais or caregiver) and record information on DCF02b.

- The nurse will find ID information on the child health card and based on the date of birth on the health card, s/he can double check if the child is eligible (age criteria) for receiving study drug.
- NB: If entering the child ID information is not working, fill in the DCF02b paper form (Appendix 3). Study nurse will **ONLY** fill Child Treatment at the health facility (Sub-study) form DCF02b paper version **WHEN** the electronic DCF02b in the **TABLET** is **NOT** working.

5.7.1.6. The nurse will advise the caregiver that in case the infant vomits within approximately 15 minutes, s/he should alert the LAKANA team so that the infant can be re-treated by the data collector. The nurse will also instruct the caregiver to seek the help of a health professional/visit a health facility if the child gets any major symptoms in the next 14 days.

- The nurse will specify to the caregiver that if the vomiting happens later than 15 minutes after drug administration, there is no need to alert the team.
- If vomiting happens at the pop-up facility, the nurse will be the one notifying the data collector.

**5.7.2.** If the data collector becomes aware that an infant has vomited soon after the study drug ingestion (within approximately 15 minutes), he will give a new, similar-size dose to the infant in question and complete form DCF02a.

## **5.8. Sample transportation to Kita lab:**

**5.8.1.** The nurse will coordinate with the driver/messenger the safe sample transportation to the Kita laboratory in appropriate time. *Refer to SOP Proc-05 (5.1.12) and SOP Proc-06 (5.1.16).*

## 5.9. Closing of the day:

- 5.9.1. After having reached the number of households/infants planned for the day, the LAKANA team will pack all the study material and return to the CSCCom.
- 5.9.2. The data collector will transmit the data to the server.
- 5.9.3. The field supervisor and nurse will manage clinical waste and remaining drugs (*see SOP Pharm-01*). The nurse will put the remaining unused sample bags at 2-8°C in the refrigerator.
- 5.9.4. The field supervisor will charge the tablet computers.
- 5.9.5. The field supervisor will report to the district supervisor on the study progress and on any issues that need to be addressed.

## 6. Occupational Safety Issues

- 6.1. The study nurse will wear disposable gloves when handling a child. S/he will wash or sanitize hands before putting on and after removing gloves. S/he will change gloves before collecting nasopharyngeal swab after collecting rectal swab sample. S/he will change gloves after each study participant.
- 6.2. All concerned study team members will handle all specimen with care and treat them as potentially infectious material. Appropriate specimen collection devices, containers, and transport media will be used to ensure optimal recovery of microorganisms and storage.
- 6.3. The study nurse will dispose of all contaminated waste (gloves, papers, swab handles, etc.) into biohazard waste bags for incineration or disposal.
- 6.4. During COVID-19 epidemic, procedures for safe and proper work will be used to reduce the risk of exposure to a hazard and prevent transmission between the study team and the study participants. Special considerations due to COVID-19 are presented in *SOP-Safety 01*.

## 7. Quality Assurance / Quality Control

The study nurse who will collect specimen will undergo practical training for rectal swab and nasopharyngeal swab sample collection. Study nurse will not be approved to collect the specimen until a supervising clinician has assessed their competency and signed off in the training log.

## 8. Appendices and other related documents

Document number	Document content
Appendix 1	Data Collection Form (DCF) 13a-AMR
Appendix 2	Sample logbook
Appendix 3	Data collection form 02b: Child Treatment at the health facility (Sub-study)
Appendix 4	Flowchart for Conducting the Enrolment visit – Sub-study visit 1

## 9. Version history, authors and approvals

Version (date)	Edits to the SOP text (author)
Version 2.0 (2021-04-20)	Added 5.6.1.4 child age and name on colored card when there are more than one child at the same age range in the same household. Added handwritten label information by study nurse. Approved by LAKANA PSG.
Version 1.0 (2021-03-23)	Authored by Laura Adubra and Yuemei Fan, in consultation with LAKANA investigators. Approved by LAKANA PSG.

**Appendix 1: Data Collection Form (DCF) 13a-AMR**

Section Header	Question Text	Question Responses	Required
Form 13a — Biological Sample Collection-AMR	Instructions: Complete this form for targeted age group children (4-14 mo and 49-59 mo children).		
	Interviewer ID (study nurse ID)		Yes
	Child ID (child ID sticker)		Yes
A. VISIT INFORMATION	1. Date		Yes
	2. MDA round (Visit number)		Yes
	3. Sample collection place	Village central place/pop-up facility	
	4. Child age group	4-14 mo   49-59 mo	Yes
B. SAMPLE COLLECTION	5. What samples collected?	Rectal swab   Nasopharyngeal swab	Yes
	6. How many rectal swabs were collected?	0   1   2   3	Yes
	6a. What time the rectal swabs were collected?		Yes
	6b. Identifier (barcode) of the first rectal swab in Cary-Blair medium tube		Yes
	6c. Identifier (barcode) of the second rectal swab in DESS medium tube		Yes
	6d. Identifier (barcode) of the third dry rectal swab		Yes
	7. How many nasopharyngeal swabs were collected in STGG media?	0   1	Yes
	7a. What time the nasopharyngeal swab was collected?		Yes
	7b. Identifier (barcode) of the nasopharyngeal swab		Yes



**Appendix 3: Data collection form 02b: Child Treatment at the health facility (Sub-study).**

Version 1.0, 08 October 2020

Section Header	Num.	Question Text	Question Responses	Required
	[0]	Instructions: This form is to be completed by the study nurse at the pop-up health facility.		
Visit information	[1]	Date		Yes
Child information	[2]	Child ID		Yes
Study drug administration	[3]	Was the child given study medication?	1, Yes   2, No, the child was sick   3, No, the child refused   4, No, the caregiver changed his / her mind   5, No, there was no drug available   6, No, other reason	Yes
	[4]	If other reason, explain		Yes (if [3], 6)
	[5]	Actual dose administered:	decimal	Yes (if [3], 1)
	[6]	Time dose administered (24-hour format):		Yes (if [3], 1)
General comments	[7]	Please record any general comments below:	text	



**Appendix 4: Flowchart for Conducting the Enrolment visit – Sub-study visit 1**

