

Standard Operating Procedures for the LAKANA trial  
**SOP Subvisit-04.: Conducting Sub-study Visits 04**  
 Version No. 1.0 (2022-03-15)

**1. Purpose and overview:**

This SOP<sup>1</sup> gives step-by-step instructions on how to conduct the sub-study visit 04 (MDA#4S<sup>2</sup>) for the mechanistic sub-study outcome measures of LAKANA in selected sub-study villages (AMR villages) near the city of Kita.

This SOP refers to SOPs Visit 01, Visit 02, Prep-02, Pharm-01, Proc-03, Proc-07, Proc-08, Safety-01, and Data Collection Form (DCF) DCF01 (e, f), DCF02, DCF02a, DCF02b, DCF03, DCF06, DCF08, DCF09, and DCF13.

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

Staff member	Responsibility
District Supervisor	<ul style="list-style-type: none"> <li>- Plans the date of entry to the village together with the study coordinator.</li> <li>- Prepares study drugs and data collector’s material and sends them from Bamako to Kita.</li> </ul>
Lab technician in Bamako	<ul style="list-style-type: none"> <li>- Prepares the QuickRead go instrument and required material (CRP and Hb measurement material and stool and dry blood spot collection material) to be dispatched from Bamako to Kita.</li> <li>- Handles and stores samples in Kita/Bamako lab.</li> </ul>
Field Supervisor	<ul style="list-style-type: none"> <li>- Communicates with the village chief and agrees on date of entry and equipment rental.</li> <li>- Works together with the nurse to transport material from Kita to the villages and Bamako.</li> <li>- Packs the data collectors’ rucksacks.</li> <li>- Makes sure all required material for visits MDA4 (v1 and v2) are in Kita one week before the entry into the village.</li> <li>- Manages disposal of study waste with study nurse.</li> </ul>
Study nurse	<ul style="list-style-type: none"> <li>- Packs sample collection equipment and material in Kita and arranges transport to the village.</li> <li>- Coordinates the setting up of the pop-up study facility in the village.</li> <li>- Completes biological sample collection form DCF13, and DCF02b in tablet computer or in paper form DCF13b (Appendix 1) and DCF02b (Appendix 3).</li> </ul>

<sup>1</sup> Abbreviations: SOP = standard operating procedure, DCF = data collection form, AMR = antimicrobial resistance, CSCCom = 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.

<sup>2</sup> MDA #4S indicates MDA round 4 for villages included in the Sub-study.

Staff member	Responsibility
	<ul style="list-style-type: none"> <li>- Completes sample logbook (Appendix 2).</li> <li>- Collects biological samples from 4-11 mo. infants.</li> <li>- Provides study drug to 4-11 mo. infants after sample collection.</li> <li>- Ensures samples are correctly labelled, transported to and deposited in Kita lab.</li> <li>- Disposes of study waste.</li> </ul>
Data collector	<ul style="list-style-type: none"> <li>- Finds the compound and households and requests permission to proceed and perform the activities.</li> <li>- Operates tablet computer - completes DCF01 (e, f), DCF02, DCF02a, DCF03, DCF06, DCF08, DCF09.</li> <li>- Gives the drug doses to 1-3 mo. infants in the household.</li> <li>- Identifies 4-11 mo. infants and advises and gives stool containers to the caregiver.</li> <li>- Measures 4-11 mo. infants, calculates dosage and writes it on the color card.</li> <li>- Provides the color cards for infants according to age.</li> <li>- Completes adverse events form DCF09 (for 4-11 mo. infants) at second visit in the village.</li> </ul>
Relais	<ul style="list-style-type: none"> <li>- Helps in finding the compounds and households.</li> <li>- Assists the data collector in study drug administration.</li> <li>- Finds, guides, and accompanies 4-11 mo. infants and caregivers to the pop-up facility if they are absent at the time of sample collection.</li> </ul>
Driver/messenger	<ul style="list-style-type: none"> <li>- Transports the nurse and sample collection material between Kita and the village.</li> <li>- Assists the nurse in setting up the pop-up facility.</li> <li>- Safely transports the samples from the village to the Kita/Bamako lab.</li> </ul>

### 3. Required materials

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>
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.

Item	Number	Specification
LAKANA card - <b>GREEN</b>	<i>As required</i>	Card for <b>9-11</b> mo. old infants.
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	2	The following questionnaire will be loaded if in village: DCF02b, DCF13, DCF09.
DCF13b, hard copy Appendix 1	<i>As required</i>	The paper version DCF13b biological sample collection form needs to be filled by study nurse for sample collection if Tablet computer or electrical 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 treatment form needs to be filled by study nurse after sample collection if Tablet computer or electrical DCF02b are not functional.
DCF09, hard copy Appendix 4	<i>As required</i>	The paper version DCF09 adverse event form needs to be filled by study nurse after sample collection if Tablet computer or electrical DCF09 are not functional.
Disposable gloves	2 pairs/participant <i>Number required to meet the daily target</i>	For cleaning the skin before and after the blood prick tests (dry blood spot on filter paper and CRP+Hb measurement)
Alcohol wipes	2 /participant <i>Number required to meet the daily target</i>	For cleaning the skin before and after the blood prick tests (dry blood spot on filter paper and CRP+Hb)
Adhesive bandage/plaster	<i>1/participant</i>	Adhesive bandage 19x72 mm
QuikRead go® instrument	1	For measuring CRP+Hb
Extra battery	1	For QuikRead go® instrument

Item	Number	Specification
QuikRead go® wrCRP+Hb reagent kit box	<i>Number required to meet the daily target</i>	For measuring CRP and Hb. 1 kit includes 50 tests with capillaries (10 µl) and plungers. Storage of unopened kit at 2-25°C until the expiry date of the kit. Unopened cuvettes after opening the foil pouch: storage at 2-8°C for 6 months, storage at 18-25°C for 3 months.
QuikRead go® wrCRP control	1	Unopened vials at 2-8°C until the expiry date. Opened vial at 2-8°C up to two months.
QuikRead go® Hb control	1	Unopened vials at 2-8°C until the expiry date. Opened vial at 2-8°C up to one months.
Dry blood spot card	<i>Number required to meet the daily target</i>	For collecting dry blood spot and later malaria PCR analyses. PerkinElmer PKI RUO Spot Saver Card
Dry Rak	<i>Number required to meet the daily target</i>	Whatman 903 DRY RAK with Velcro, safely and properly air-drying multiple collected DBS specimen cards in a suspended horizontal position.
Indicating desiccant packet	2 desiccant/zip lock bag <i>Number required to meet the daily target</i>	QIAGEN WB100003, 1 g, to keep the DBS card dry in the bag during transport/storage. Desiccant change from blue to pink to indicate absorption of moisture.
Plastic zip lock bag	1/DBS card	To pack DBS card for transport.
Stool container	<i>Number required to meet the daily target</i>	For collecting whole stool sample. Sterile Faeces Container includes a spoon, 60ml (red cap with a spoon)
Stool collection instructions for caregivers, hard copy, Appendix 5	<i>Number required to meet the daily target</i>	For instructing caregivers to collect whole stool samples from 4-11 mo. infants the day before they visit the pop-up facility to have DBS sample collected and CRP and Hb measured (two visits, 14 days apart)
Disposable diaper	1 diaper/participant <i>Number required to meet the daily target with different size</i>	For collecting whole stool sample. Muumi 2-5 kg, 5-8 kg and 7-14 kg
Nappy liner	1 sheet/participant	For collecting whole stool sample.

Item	Number	Specification
	<i>Number required to meet the daily target</i>	
Extra bag of DBS cards	1 bag/village	Extra bag of DBS cards – one bag of DBS cards (20pcs) for DBS specimen collection
Extra bag of desiccant	1 bag/village	Extra bag of desiccants – one bag of desiccants (20pcs) for DBS specimen collection
Extra bag of stool containers	1 bag/village	Extra bag of stool containers (10pcs) for whole stool specimen collection
Printed barcode label	1 printed label/stool container (126 labels/ sheet) <i>Number required to meet the daily target</i>	For collected whole stool sample, the nurse will affix the label to the contained when received in pop-up facility and fill the participant information and scan the barcode (or manually enter if scanning is not working) to tablet
Cooler box	2	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™ Traceable Thermometer <u>14-648-26</u> )
Paper towel	1 towel/participant <i>Number required to meet the daily target</i>	For cleaning surfaces
Biohazard waste bag	2/village/day	For sample collection and cleaning waste
70% ethanol	2 bottles	500 – 1000 ml
Surgical mask/ N-95 mask	<i>Number required to meet the daily target</i>	
Goggles or face shield	1/nurse	For nurse in close contact with patients
Refrigerator	1	To store and maintain transport media at appropriate temperature (2-8°C) and prepare/store ice packs to be used for maintaining cooler boxes.
Lancets for heel prick blood collection	1/participant	For making the skin incision for blood collection. DBS sample collection and blood for measuring CRP and Hb. Blood

Item	Number	Specification
		lancets VITREX® STERIHEEL® Baby II, 2.00 x 3.00 mm

#### 4. Definitions and general instructions

##### 4.1 Definitions

4.1.1. District supervisor: a LAKANA staff member coordinating trial activities at the district level. The district supervisor reports primarily to the study coordinator and is stationed in the district office.

4.1.2. Field supervisor: a LAKANA staff member responsible for coordinating data collection teams' activities. She/he is under the supervision of the District supervisor.

4.1.3. Lab technician: a LAKANA staff member based in Bamako or Kita (Bamako or Kita lab), and responsible for preparing sample collection material for study nurse and handling specimens brought from villages.

4.1.4. Study nurse: a LAKANA staff member responsible for AMR and mechanistic sub-study sample collection. The study nurse has to be the same person in all activities.

4.1.5. Data collector: a LAKANA staff member collecting data at the compound, household, and individual level. The data collector has to be the same person in all activities.

4.1.6. Relais Communautaire: a volunteer chosen by the community who serves as a bridge between professional health staff and the villagers.

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 the mechanistic sub-study: a child aged **4-11 mo.** living in a household that consented to participate in the LAKANA trial. Consent for participation in the Sub-study will be requested from the head of each 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. Driver: a hired person that drives the sample collection materials, samples, and nurse between Kita/Bamako and the village, and assists the nurse in setting up the pop-up facility.

4.1.11. 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. This sub-study visit 4 includes two visits with two activities in each:**

#### **4.2.1.1. Visit s4-v1 (sub-study visit 4 – village visit 1):**

##### **In the first activity of the FIRST visit (first day):**

All mechanistic study eligible infants will be identified. Stool containers, nappy liner, disposable diaper and instructions will be given to caregivers on collecting stool samples.

##### **In the second activity of the FIRST visit (second day):**

All main study eligible infants (1-11 mo.) will be treated with study drug. Mechanistic study eligible infants (4-11 mo.) will be treated in the pop-up facility the day after receiving the stool samples, measuring CRP+Hb and collecting DBS samples from heel prick blood from these infants.

#### **4.2.1.2. Visit s4-v2 (sub-study visit 4 – village visit 2):**

Happens 2 weeks after visit s4-v1 in the village.

##### **In the first activity of the SECOND visit (first day):**

The **SAME** infants aged 4-11 mo. from the FIRST visit will be identified and stool sample containers, nappy liner and disposable diaper will be given to caregivers.

##### **In the second activity of the SECOND visit (second day):**

Infants will be identified and accompanied to the pop-up facility and samples (the same as collected 2 weeks prior) will be collected again.

The locations, timing, and samples collected are described in a figure in Appendix 6.

**4.2.2.** For visits s4-v1 and s4-v2 there will be four main processes: 1) Preparatory activities, 2) Data collectors visit to a household, 3) Biological samples collection in a central site in the village, and 4) Post-village activities. The activities for each process are illustrated in Figure 1. and Figure 2. below. The step-by-step actions are elaborated in section 5.

Figure 1. Flow chart of visit s4-v1

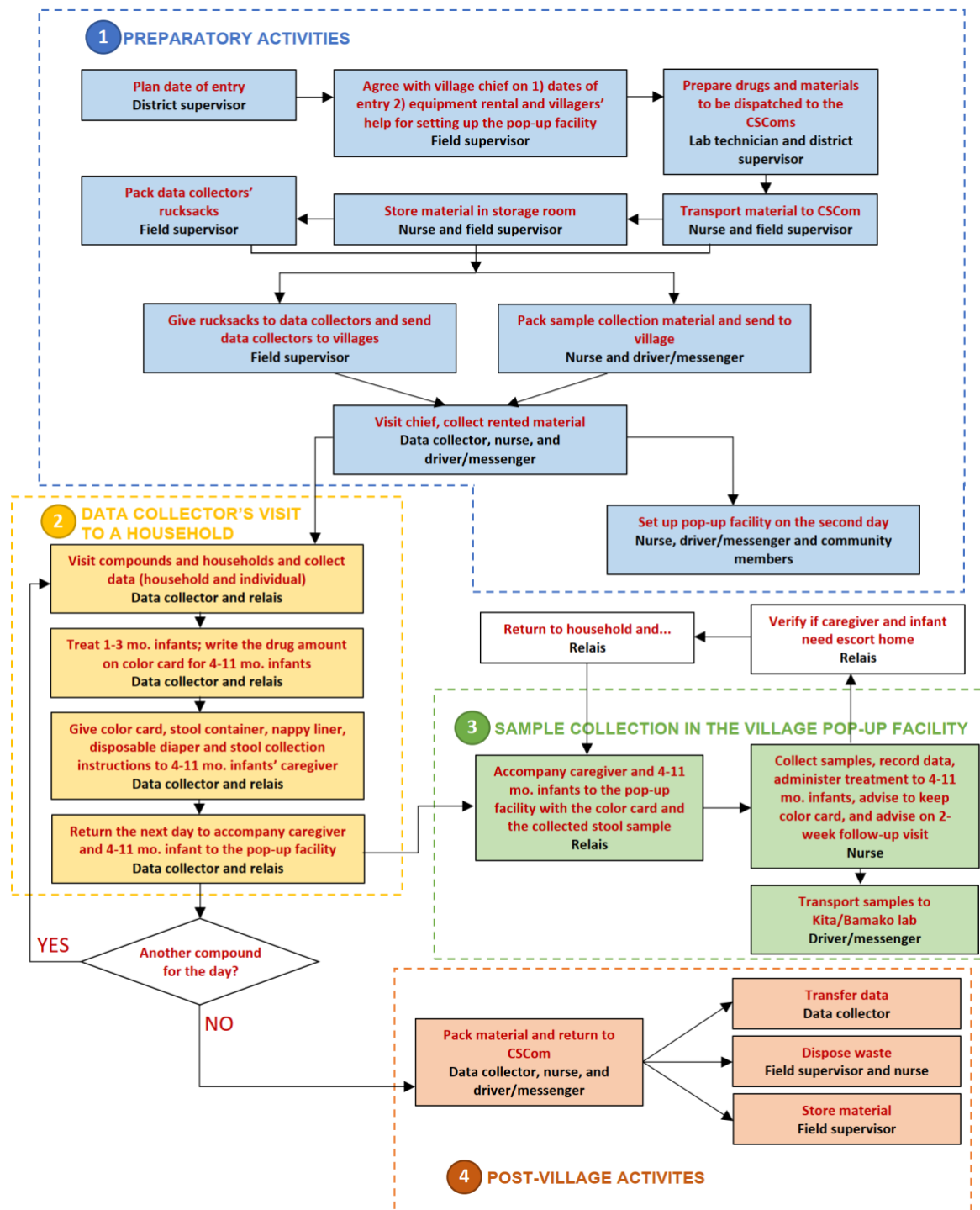
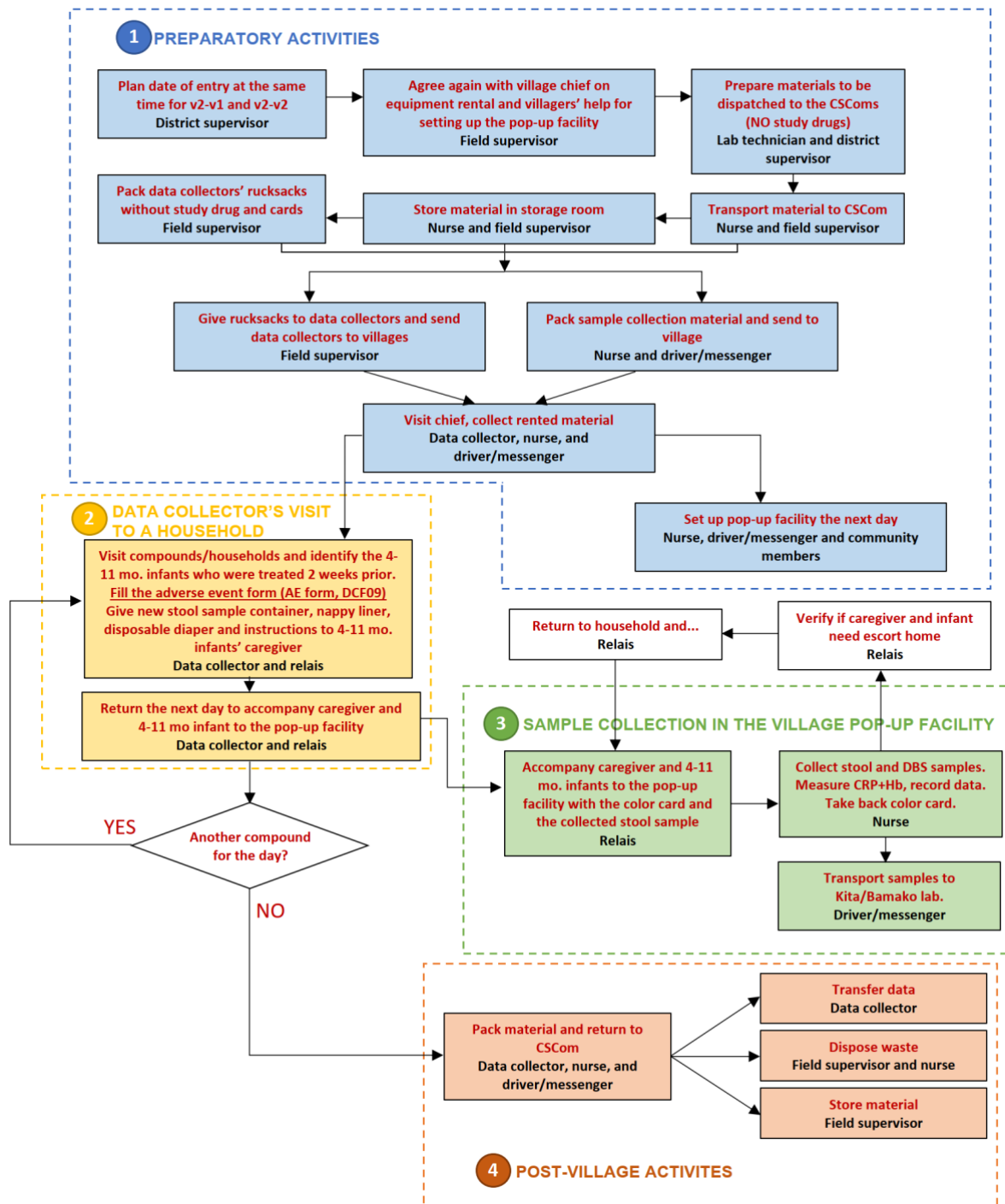




Figure 2. Flow chart of visit s4-v2



## **5. Step-by-step procedures**

### **5.1. Visit s4-v1 (sub-study visit MDA4 – village visit 1) (see also Appendix 6)**

#### **5.1.1. Plan date of entry (District supervisor):**

**5.1.1.2.** 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. The date of the follow-up visit (in 2 weeks) will be agreed upon as well.

#### **5.1.2. Agree with village chief (Field supervisor):**

**5.1.2.1.** Prior to entry in a village (~1 week), the field supervisor will agree with the chief of the village on the dates of entry. At this occasion, the field supervisor will discuss (for both visits) 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.

**5.1.2.2.** The field supervisor will explain the purpose of the mechanistic sub-study 4 visits and that the visit will be repeated for sample collection 2 weeks after the initial visit. The samples collected will be explained to prevent rumors.

#### **5.1.3. Prepare material for Kita (Lab technician and district supervisor):**

**5.1.3.1** At the Bamako lab (~1 week prior to date of entry in village), the lab team will prepare the QuikRead Go® instrument including one battery, extra battery, wrCRP+Hb reagent kit box, CRP and Hb controls and other the sample collection material for measuring CRP+Hb, DBS and stool samples to be dispatched to the Kita district office. Packing of material is described in *SOP Proc-07*.

**5.1.3.2.** 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 village. *Refer to SOP Pharm-01 for details on drug management.*

#### **5.1.4. Transport material from Kita to village (Nurse and field supervisor):**

**5.1.4.1.** The day before entry in a village, the nurse and field supervisor will pack the material prepared and arrange the transportation to the village. The quantity of study drugs to be picked up will be estimated by the field supervisor. During transportation, the QuikRead Go® CRP+Hb reagent kit box and CRP and Hb controls will be kept at 2-8°C.

**5.1.4.2.** The nurse and field supervisor will store the material in the LAKANA storage room in Kita. The storage room is equipped with a refrigerator where the nurse will store the QuikRead Go® reagent kit box and CRP and Hb controls at 2-8°C.

**i.** 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).

ii. When going to the village, the nurse will keep the QuikRead Go® reagent kit box and CRP and Hb controls at 2-8°C in the electric cooler box.

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

**5.1.5. Entry in a village:**

**5.1.5.1.** On the morning of the date of entry in a village, the field supervisor will prepare the data collector rucksacks (*Refer to SOP Visit-01 for details*). The study nurse will pack the sample collection material needed for the day.

**5.1.5.2.** The whole team will move together to the village. The data collector has his/her own vehicle and a LAKANA driver will transport the nurse, the field supervisor, and the sample collection material.

**5.1.5.3.** The field supervisor will visit the data and sample collection team to provide technical support and to distribute the data collector rucksacks.

**5.1.5.4.** 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 **on the second day of the visit**. The rented materials (1 table and 3 chairs) will be provided. The LAKANA team will request assistance in setting up the pop-up facility.

**5.1.5.5.** The data collector accompanied by two Relais will start visiting compounds/households.

**5.1.5.6.** The nurse, the driver and the community members will set-up the pop-up facility on the second day and the subsequent days.

**5.1.6. Data collection in household, identification of sub-study eligible infants, and treatment of 1-3 mo. old infants (Data collector):**

**5.1.6.1.** The data collector will follow the procedure described in *SOP-Visit 02* section 5.2. for conducting subsequent household visit with some exceptions:

- i. An additional form DCF08 will be filled for 4-14 mo. children.
- ii. For 4-11 mo. old infants in the treatment form the data collector will select the answer “Study Nurse” to the question “Who is planned to give medication”.

**5.1.6.2.** Consent for participation in Sub-study: The data collector will seek consent to participate in the sub-study from the head of the household.

**5.1.6.3. LAKANA cards:** The data collector will issue colored LAKANA cards to children eligible for the Sub-study. **These cards will not be returned after visit s4-v1. They will be returned only after s4-v2.** In the household, the data collector will give:

**Yellow** card to **4-5** mo. old infants for whom there is a consent to participate in Sub-study.

**Blue** card to **6-8** mo. old infants for whom there is a consent to participate in Sub-study.

**Green** card to **9-11** mo. old infants for whom there is a consent to participate in Sub-study.

**5.1.6.4. 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*) **or the vaccination card**. 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. **The color card will be given to the head of the household for safekeeping.**

**5.1.6.5. Treatment:**

- i.** The data collector will prepare and administer the study drug **ONLY** to eligible **1-3 mo. old infants** for whom there is a caregiver consent for treatment. *Refer to SOP-Proc 1 for procedure on study drug Administration.*
- ii.** For **4-11 mo. old infants**, if consent 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 by the nurse later the next day. The data collector will **NOT prepare the study drug** for this age group. The data collector will write the dose on the color card.
- iii.** The data collector will give a stool sample container, a disposable diaper and a sheet of nappy liner to the caregiver of all 4-11 mo. infants and advise on how to collect the stool sample. The data collector will also write the infant's name and ID sticker number on the stool container.
- iv.** The data collector will record all the 4-11 mo. infants who are eligible for the mechanistic sub-study on the registry book, keep the list and make sure to find the same infant when they come back for the second visit after 14 days.

**5.1.6.6.** The data collector will continue with his activities in the households/compound (repeat step 5.1.6).

**5.1.6.7.** At the end of the day, the data collector will check on the tablet computer and paper registry which households (visited during the day) had infants aged 4-11 months and start visiting them the next day in the same order as the first day. The second day the data collector will first visit the households with 4-11 mo. infants and the Relais will accompany them to the pop-up facility.

**5.1.7. Data and sample collection at pop-up health facility and treatment of 4-11 mo. old infant (Nurse):**

**5.1.7.1.** Every time a data collector/Relias will arrive at the pop-up facility with an eligible child and her/his caregiver for sample collection:

The nurse will open a new record (DCF13b, Appendix 1) 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 and scanned into tablet or manually entered if scanning is not working.

**5.1.7.2.** 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 procedures and give instructions to the caregiver.

**5.1.7.3.** The nurse will collect the stool sample and DBS samples, measure CRP+Hb (*refer to Proc-8 on how to measure CRP+Hb and collect DBS and stool sample*) and record information on the tablet or DCF13b manually if tablet is not working.

**i.** 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 – affix one barcode label to the collected stool sample container, scan the barcode on the container/or manually enter to the tablet. Collect DBS sample, scan the barcode on the card/or manually enter to the tablet. Measure blood CRP+Hb and record the results into the tablet.

**ii.** If the caregiver did not collect the stool sample in the container given the day before, the nurse will ask the caregiver and infant if they can wait at the pop-up facility until a stool sample is collected or come back the next day with a stool sample.

**iii.** If they do not bring a stool sample the next day, there will be no stool collection for that infant. All other samples will be taken.

**5.1.7.4.** After samples are collected and information entered in the tablet, the nurse will give back the color card to the caregiver and advise the caregiver to not lose it and to give it to the head of the household for safekeeping.

**5.1.7.5.** The nurse will treat the eligible 4-11 mo. old infant with the dose written on the color card by the data collector and record information on treatment form (DCF02b, Appendix 3).

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.

**5.1.7.6.** 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.

- i.** 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.
- ii.** If vomiting happens at the pop-up facility, the nurse will be the one notifying the data collector.

**5.1.7.6.** 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.

**5.1.8. Sample transportation to Kita/Bamako lab (Driver):**

**5.1.8.1.** The nurse will coordinate with the driver the safe sample transportation to the Kita/Bamako laboratory in appropriate time. The DBS have to stay dry and the stool samples should be kept at 2-8 °C.

**5.1.9. Closing of the day:**

**5.1.9.1.** After having reached the number of households/infants planned for the day, the LAKANA team will pack all the study material and return to Kita.

**5.1.9.2.** The data collector will transmit the data to the server.

**5.1.9.3.** The field supervisor and nurse will manage clinical waste and remaining drugs (*see SOP Pharm-01*). The nurse will put the remaining unused sample material at 2-8°C in the refrigerator.

**5.1.9.4.** The field supervisor will charge the tablet computers and the nurse will charge the QuikRead go® instrument.

**5.1.9.5.** The field supervisor will report to the district supervisor on the study progress and on any issues that need to be addressed.

**5.2. Visit s4-v2 (sub-study visit 4 – village visit 2)**

**5.2.1. Date of entry and study personnel (District supervisor):**

**5.2.1.1.** The date of entry was planned in beforehand and was informed to the staff.

**5.2.1.2.** If possible, the nurse and data collector(s) will be the same persons as in visit s4-v1.

**5.2.2. Agree with village chief (Field supervisor):** the follow-up visit date was agreed with the village chief earlier, but the field supervisor will be in contact with the chief (~1 week) prior to the follow-up visit and assure that the material can still be rented, and that the community can help with setting up the pop-up facility.

**5.2.3. Preparing material (Lab technician and district supervisor):**

**5.2.3.1.** For the follow-up visit s4-v2, prior to entry in a village (~1 week), the field supervisor will check that all required materials are in Kita (the same material as in section 5.1.3, but without study drugs).

**5.2.3.2.** If some material is missing in Kita, the field supervisor will inform Bamako lab. Bamako lab will then prepare the sample collection material and send to Kita district office (similar to visit s4-v1).

**5.2.4. Transport material from Kita to the village and store (Nurse and field supervisor):**

**5.2.4.1.** The day before entry in a village, the nurse and field supervisor will pack the material prepared and arrange the transportation to the village.

**5.2.4.2.** No study drug will be picked up for this visit. During transportation, the QuikRead Go® reagent kit box and CRP and Hb controls will be kept at 2-8°C.

**5.2.4.3.** The nurse and field supervisor will store the material in the designated storage room in Kita. The storage room is equipped with a refrigerator where the nurse will store the QuikRead Go® reagent kit box and CRP and Hb controls at 2-8°C.

When going to the village, the nurse will keep the QuikRead Go® reagent kit box and CRP and Hb controls at 2-8°C in the electric cooler box.

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

**5.2.5. Entry in a village actions are identical to the first visit (see section 5.1.5)**

**5.2.6. Household entry and identification of sub-study enrolled children (Data collector):**

**5.2.6.1.** The data collectors will check the list of households with 4-11 mo. infants and enter the households as is described in *SOP-Visit 02* but will **NOT initiate data collection** as per usual. They will only identify the infants aged 4-11 months, give their caregivers a stool container, a disposable diaper and a nappy liner, advise again on how to collect the stool sample.

**5.2.6.2.** The data collectors will open the adverse events form (DCF 09, Appendix 4) to collect the incidence of adverse events (AE) within 14 days of study drug administration from the caregivers with the infants who has received the drug in the first visit.

**5.2.6.3.** Whether or not the infant was treated 2 weeks prior (a LAKANA color card was given to the caregiver) determines whether or not samples will be taken, not the age of the child during the follow-up visit (s4-v2). ID stickers from the initial visit (s4-v1) will be used (ID sticker either in the LAKANA card or in the child health card).

**5.2.6.3.** Identical to section 5.1.6.7.

**5.2.7. Data and sample collection at pop-up facility (Nurse):**

**5.2.7.1.** This step will be identical to previous visit s4-v1 sections 5.1.7.1 to 5.1.7.3.

**5.2.7.2.** After samples are collected and information entered in the tablet, the nurse will collect back the LAKANA color cards.

**5.2.8. Sample transportation to Kita/Bamako lab and closing the day will be identical to s4-v1 (sections 5.1.8 and 5.1.9).**

**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 start by collecting the DBS+CRP+Hb and change gloves if the gloves are very bloody before taking the stool sample. If stool sample is taken first for some reason, then hands will be sanitized, and gloves changed before taking blood 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 storage.

**6.3.** The study nurse will dispose of all contaminated waste (gloves, papers, tubes etc.) into biohazard waste bags for incineration or disposal.

**6.4.** During the COVID-19 pandemic, 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 stool and blood 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**



<b>Document number (Version)</b>	<b>Document content</b>
Appendix 1	Data Collection Form (DCF) 13b-mechanistic sub-study
Appendix 2	Sample logbook
Appendix 3	Data collection form 02b: Child Treatment at the health facility (Sub-study)
Appendix 4	Data collection form 09: Adverse events
Appendix 5	Stool collection instructions
Appendix 6	LAKANA sub-study visit flow chart for visit 4

### 9. Version history, authors and approvals

<b>Version (date)</b>	<b>Edits to the SOP text (author)</b>
0.1. (2022-03-01)	Rikhard Ihamuotila in consultation with Yuemei Fan, Per Ashorn, Laura Adubra, and Ulla Ashorn based on Yuemei Fan's and Laura Adubra's SOPs (main study visit 1 and sub-study visit 1)
1.0. (2022-03-15)	Rikhard Ihamuotila in consultation with Yuemei Fan, Per Ashorn, Laura Adubra, and Ulla Ashorn based on Yuemei Fan's and Laura Adubra's SOPs (main study visit 1 and sub-study visit 1)

**Appendix 1: Data Collection Form (DCF) 13b-mechanistic sub-study**

Version 0.1, April 11, 2021

Section Header	Question Text	Question Responses	Required
Form 13b — Biological Sample Collection-mechanistic sub-study	Instructions: Complete this form for targeted age group children.		
	Interviewer ID (study nurse ID)		Yes
	Child ID (child ID sticker)		Yes
A. VISIT INFORMATION	1. Date		Yes
	2. MDA round (Visit number)	4S-00 / 4S-14	Yes
	3. Sample collection place	Village central place/pop-up facility	
	4. Child age group	4-11 mo	Yes
B. SAMPLE COLLECTION	5. What samples collected?	Heel prick blood CRP   Heel prick blood Hb   Heel prick blood, blood spot   Stool	Yes
	6. Was a heel prick blood sample collected?	Yes   No	Yes
	6a. Record the result of CRP	CRP =	Yes
	6b. Record the result of Hb	Hb =	Yes
	7. How many blood spots were stored on filter paper card?	0   1   2	Yes
	7a. Identifier (barcode) of the filter paper card?		Yes
	8. Was a stool sample collected?	Yes   No	Yes
	8a. What time the whole stool sample was collected?		Yes
	8b. What date and time did the child pass the stool?		Yes
	8c. Identifier (barcode) of the stool sample		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: Data collection form 09: Adverse Events**

Version 1.0, 08 October 2020

Purpose: Active surveillance for the incidence of adverse events (AE) within 14 days of study drug administration, in the 60 villages selected for more detailed data collection on outcomes other than mortality.

Section Header	Num.	Question Text	Question Responses	Required
	[0]	Instructions: Complete this form for targeted age group children.		
	[1]	Interviewer ID		
	[2]	Child ID		
Visit information	[3]	Date:		
Symptoms	[4]	Check the symptoms experienced in the last 14 days:		
	[5]	Diarrhea	0, None   1, Mild   2, Moderate   3, Severe/Life threatening	Yes
	[6]	On how many days did <name> experience diarrhea?	<i>integer</i>	Yes (if [5] != 0) <i>max=14</i>
	[7]	Loose stools	0, None   1, Mild   2, Moderate   3, Severe/Life threatening	Yes
	[8]	On how many days did <name> experience loose stools?	<i>integer</i>	Yes (if [7] != 0) <i>max=14</i>
	[9]	Vomiting	0, None   1, Mild   2, Moderate   3, Severe/Life threatening	Yes
	[10]	On how many days did <name> experience vomiting?	<i>integer</i>	Yes (if [9] != 0) <i>max=14</i>
	[11]	Rash-itching	0, None   1, Mild   2, Moderate   3, Severe/Life threatening	Yes
	[12]	On how many days did <name> experience Rash-itching?	<i>integer</i>	Yes (if [11] != 0) <i>max=14</i>
	[13]	Swelling of the lips	0, None   1, Mild   2, Moderate   3, Severe/Life threatening	Yes

	[14]	On how many days did <name> experience Swelling of the lips?	<i>integer</i>	Yes (if [13] != 0) <i>max=14</i>
	[15]	Difficulty breathing- wheeze	0, None   1, Mild   2, Moderate   3, Severe/Life threatening	Yes
	[16]	On how many days did <name> experience difficulty breathing- wheeze?	<i>integer</i>	Yes (if [15] != 0) <i>max=14</i>
	[17]	Crying more than usual	1, Yes   0, No	Yes
	[18]	Did the child experience other symptoms?	1, Yes   0, No	Yes
	[19]	If yes, describe symptoms		Yes (if [18] = 1)
	[20]	What was the outcome of the event (s) reported?	1, Child was hospitalized (Fill out Suspected SAE Form)   2, Child was seen as an outpatient and returned home   3, Other	
	[21]	Specify Other		

## Appendix 5. Stool collection instructions

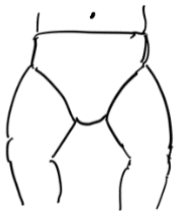
### STOOL COLLECTION INSTRUCTIONS



Do the following activities tomorrow in the morning.



Put the nappy liner on the inside of the nappy where the child will probably pass the stool.



Put on the nappy.



Take off the nappy when the child has passed stool.



Collect or pour all the stool in the container.



Mix the stool and keep the stool container in the dark and inside in a place with room temperature.



Dispose of the nappy and nappy liner.

**Appendix 6. LAKANA sub-study visit flow chart for visit 4**

