

Standard Operating Procedures for the LAKANA trial  
**SOP Proc-02: SAE Reporting, Recording and Notification**  
 Version 4.0 (2023-06-21)

**1. Purpose and overview:**

The purpose of this SOP<sup>1</sup> is to describe the process, and requirements, for reporting, recording and notifying Serious Adverse Events (SAE) occurring in the context of LAKANA azithromycin MDA. This SOP refers to data collection forms (DCF) DCF10a, DCF10b, DCF11, DCF12, and the Investigator Sponsored Research (ISR) SAE form.

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

Staff member	Responsibility
Directeur Technique de Centre (DTC)	<ul style="list-style-type: none"> <li>- Records all deaths and hospitalization among 1-11-month-old infants at the CSCoM.</li> </ul>
Data collector/nurse	<ul style="list-style-type: none"> <li>- Makes sure the caregiver notifying a suspected SAE has visited/contacted a health facility (if applicable)– and if not, recommends it.</li> <li>- Performs an investigation of the event to determine the information needed to complete Form DCF10a on tablet computer.</li> <li>- Completes Form DCF10a and transmits the data to the server.</li> <li>- Calls his supervisor to notify the suspected SAE and the data transmitted.</li> </ul>
Supervisor	<ul style="list-style-type: none"> <li>- Makes sure the caregiver notifying a suspected SAE has visited/contacted a health facility (if applicable)– and if not, recommends it.</li> <li>- Identifies a suspected SAE based also on events reported by CSCoM personnel.</li> <li>- Performs an investigation of the event to determine the information needed to complete Form DCF10a on tablet computer.</li> <li>- Completes Form DCF10a and transmits the data to the server.</li> <li>- Calls the study coordinator to notify all suspected SAEs and the data transmitted.</li> </ul>

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<sup>1</sup> SOP = standard operating procedure, LAKANA = Large-scale Assessment of the Key health-promoting Activities of two New mass drug administration regimens with Azithromycin, SAE = Serious Adverse Event, DCF = Data Collection Form, ISR = Investigator Sponsored Research, DTC = Directeur Technique de Centre, DSU = Drug Safety Unit, DSMB = Data Safety and Monitoring Board, CSCoM = Centre de Santé Communautaire, MDA = Mass Drug Administration, PI = Principal Investigator.

	<ul style="list-style-type: none"> <li>- Follows the SAE until resolution or stability-completes Form DCF11 and transmits the data to the server.</li> </ul>
Study Coordinator	<ul style="list-style-type: none"> <li>- Retrieves and reviews Form DCF10a transmitted to the server by site study personnel</li> <li>- Determines relatedness of event to study drug, characterises suspected SAEs and completes Form DCF10b.</li> <li>- Retrieves and reviews Form DCF11 transmitted to the server by site study personnel.</li> <li>- Ensures that the SAE is followed until resolution or stability.</li> <li>- Completes Form DCF12.</li> <li>- Reports all suspected SAEs to principal investigators (PI &amp; Co-PIs) or designee: <ul style="list-style-type: none"> <li>- Prints the ISR SAE Form (manually or with the data collection system, as applicable).</li> <li>- Transmits the ISR SAE Form to Malian co-PI or designee and Finnish PI.</li> </ul> </li> <li>- Makes sure that the ISR SAE Form is transmitted to Pfizer within the required timelines.</li> </ul>
Malian Co-Principal Investigator	Reviews the ISR SAE Form and submits to Pfizer local Drug safety Unit (DSU).

### 3. Required materials

Item	Number	Specification
Tablet computer – for data collector/nurse	1	The following questionnaire will be loaded: DCF10a - Initial Report of a Suspected Serious Adverse (Part 1)
Tablet computer - for supervisor	1	The following questionnaires will be loaded:

Item	Number	Specification
		DCF10a - Initial Report of a Suspected Serious Adverse (Part 1) DCF11 - Follow up Report of a Suspected Serious Adverse
Computer – for study coordinator	1	The following questionnaires will be loaded: DCF10b - Initial Report of a Suspected Serious Adverse (Part 2) DCF12 - Suspected Serious Adverse Event Conclusion
Pad to note any concern	As required	
Pen	As required	
Personal Protective Equipment (PPE) individual kit	1	1 Kit/ LAKANA staff member (For details on the kit composition and utilization, refer to <i>SOP-Safety 01 Hygiene and PPE</i> )

#### 4. Definitions and general instructions

##### 4.1. Definitions

**4.1.1.** Study drug: Azithromycin or placebo powder -produced by Pfizer- packed in non-opaque, plastic bottles. Study drug bottles are labelled with a letter code. At any village (cluster), all infants will receive study drug of the same letter code (for each cluster, we will use bottles with two letter codes, one for visits between January and June and the other one for visits between July and December).

**4.1.2.** Serious Adverse Event (SAE): A SAE is any adverse event that:

- Results in death of a participant. NB: Deaths that occur more than 14 days after an MDA or that become known through interviews at the study MDAs (i.e., every 3 months) will not be considered suspected SAEs, as they will be reported as primary outcomes. In these cases, no suspected SAE form will be filled in or submitted to Pfizer, Malian IRB or DSMB.
- Is life-threatening (i.e., causes an immediate risk of death) for a participant.

- Requires inpatient hospitalization or prolongation of existing hospitalization of a participant. Hospital inpatients are patients who are admitted to a hospital ward, and the admission must span at least one midnight.
- Results in persistent or significant disability or incapacity of a participant.
- Is considered an important medical event by a study physician.

**4.1.3.** Adverse event: an AE is any untoward medical occurrence in a LAKANA trial participant administered a study drug, which is not considered a SAE.

**4.1.4.** Active Surveillance of AEs and SAE: in LAKANA, an active surveillance system is one where the caregivers of infants participating in the study are invited to the project temporary facilities (“pop-up facility” in the village) at a given MDA and questioned about any major events a child experienced after receiving the study drug. The active surveillance system to determine the incidence of AEs and SAEs within 14 days of study drug administration will be in place in the 59 villages selected for more detailed data collection on outcomes other than mortality. On MDA4 data collectors will collect information on any symptoms and their severity (diarrhea, loose stools, vomiting, Rash-itching, Swelling of the lips, Difficulty breathing- wheeze, Crying more than usual, or other self-reported symptoms) experienced within 14 days of drug administration (a +/- 4 days window is allowed for conducting the follow-up visit where the DCs will collect data on AEs). If the outcome of the adverse event (s) reported is that the child was hospitalized or if an SAE is suspected, the data collectors/nurses will start an SAE investigation (as described later in the text, see [4.2.1](#)).

**4.1.5.** Passive Surveillance of SAE: in LAKANA, a passive surveillance system refers to the reliance on community members and local health facilities (CSComs) to receive data on suspected SAE among 1-11 months old infants whilst an MDA is implemented in a village. There is no active search for SAE. The passive surveillance system to determine the incidence of SAEs within 14 days of study drug administration will be in place in the whole study area (1152 villages).

## **4.2. General instructions**

**4.2.1.** Active surveillance of AE and SAE - applicable only for the sub-study. The LAKANA staff will invite at the pop-up health facilities, 4-11 months old infants and their caregivers at 9 months after enrollment (MDA 4 for biological sample collection. At these visits, a study nurse will also interview the caregivers about symptoms that the infants have experienced after receiving the study drug. If a SAE is suspected, the nurse will complete **Form DCF10a-Initial Report of a Suspected Serious Adverse Event**.

**4.2.2.** Passive surveillance of SAE: data collectors will instruct caregivers to alert a Relais or a LAKANA data collector or supervisor if a child experiences, **within**

**two weeks of mass treatment**, a serious adverse event (by the definition in section 4.1.2).

- 4.2.2.1. Whenever the LAKANA staff (data collector or supervisor) receives a call about a suspected SAE, the staff will first make sure that the caregiver has already sought professional medical care— and if not, will recommend it. The LAKANA staff member will complete **Form DCF10a-Initial Report of a Suspected Serious Adverse Event**.
- 4.2.2.2. Passive surveillance of SAE will also be done through health facilities: whilst a village MDA is being implemented and for two weeks thereafter, the DTC will record any major events (deaths, hospitalizations) among 1-11-month-old infants and will report to a LAKANA supervisor on each weekday. If a SAE is suspected, the supervisor will complete **Form DCF10a-Initial Report of a Suspected Serious Adverse Event**
- 4.2.3. The study coordinator will report all suspected SAEs (ISR SAE Form) to the Malian co-PI and copy the Finnish PI.
  - 4.2.3.1. The Malian co-PI will review the form and he (or his designee) will submit the **ISR SAE Form to Pfizer within one business day of the study coordinator's first awareness of the suspected SAE**. The Malian Co-PI or his designee will also forward the **ISR SAE Form submitted to Pfizer to the Finnish PI**.
  - 4.2.3.2. The Malian Co-PI or his designee will also forward the ISR SAE Form to the **Malian IRB FMPOS within 72h day of the study coordinator's first awareness of the suspected SAE**.
  - 4.2.3.3. The Finnish PI will forward the ISR SAE Form to the **Data Safety and Monitoring Board (DSMB)**, according to the recommendations by the chair of the DSMB.

## 5. Step-by-step procedures (Appendix 1)

### 5.1. Recording– Initial Report (Part 1)

- 5.1.1. If a study nurse (Sub-study) suspects a SAE, s/he will complete **Form DCF10a-Initial Report of a Suspected Serious Adverse Event** on the tablet computer to collect initial information on the event. S/he will transmit the data to the server and call a LAKANA supervisor to notify the suspected SAE. The supervisor will in turn call the study coordinator who will proceed as described in section [5.2](#).
- 5.1.2. Based on instructions presented to the caregiver at an MDA visit, the caregiver may call a study staff member (data collector or supervisor) in the 14 days following the visit. If the study staff member suspects a SAE, s/he will complete **Form DCF10a-Initial Report of a Suspected Serious Adverse Event**.

5.1.2.1.If the person filling the form is a data collector, s/he will transmit the data to the server and call the supervisor to notify the event. The supervisor will in turn call the study coordinator who will proceed as described in section [5.2](#).

5.1.2.2.If the person filling the form is a supervisor, s/he will transmit the data and notify the study coordinator who will proceed as described in section [5.2](#).

**5.1.3.** Whilst a village MDA is being implemented and for two weeks thereafter, the DTC will be in charge of 1) recording any major events (deaths, hospitalizations) among 1-11-month-old infants and 2) sending a text on each weekday to the LAKANA supervisor to report (if none of the events occurred, the DTC will still text the LAKANA supervisor to report that no event occurred).

5.1.3.1.If any of the events listed above occurred, the supervisor will visit or call the concerned households and investigate. If the concerned infant participated in the latest MDA and if the supervisor suspects a SAE, s/he will complete **Form DCF10a-Initial Report of a Suspected Serious Adverse Event**. S/he will transmit the data and notify the study coordinator who will proceed as described in section [5.2](#).

## **5.2. Recording– Initial Report (Part 2)**

**5.2.1.** Upon receipt on the server of Form DCF10a, the study coordinator will review the form and complete **Form DCF10b-Initial Report of a Suspected Serious Adverse Event (Part 2)**.

5.2.1.1.If the child did not receive study drug within 14 days before symptoms onset, the event will not be considered a suspected SAE.

5.2.1.2.If the child did receive study drug within 14 days before symptoms onset, the event will be considered a suspected SAE. The study coordinator will complete the following section: Suspected SAE characteristics and Preliminary causality assessment.

**5.2.2.** If form **DCF10b** conclude to a suspected SAE:

5.2.2.1.the child has recovered or died, the study coordinator will proceed to Form **DCF12-Suspected Serious Adverse Event Conclusion** (see [5.5](#)), print the **ISR SAE Form** and transmit to the Malian co-PI (with the Finnish PI in copy) for review, validation, and submission purposes.

5.2.2.2.the child is still ill (not recovered, not dead), the study coordinator will transmit the **ISR SAE Form** (which is completed based on the information retrieved from the LAKANA forms) to the Malian co-PI (with the Finnish PI in copy) for review, validation, and submission purposes. The supervisor will continue monitoring the participant's health on a **daily** basis (see [5.4](#)).

## **5.3. Notification to Pfizer – First Notification**

**5.3.1.** The Malian co-PI (or the study coordinator) will submit the **ISR SAE Form** to the Pfizer DSU at to [MAR.AEReporting@pfizer.com](mailto:MAR.AEReporting@pfizer.com). To submit the ISR SAE Form to Pfizer DSU, there are two possible channels of communication:

5.3.1.1. The study co-PI (or the study coordinator) will use the **Kiteworks application** (see Appendix 2).

- NB: The Kiteworks application can only be used to send mail to Pfizer addresses (the Finnish PI cannot be copied to the communication) thus the study co-PI (or the study coordinator) will send a separate regular e-mail to share the ISR SAE form with the Finnish PI.

5.3.1.2. The Mali study co-PI (or the study coordinator) will use a password-protected e-mail (the user needs to send the password separately to the recipient).

**5.3.2.** Reporting days (Monday to Friday): the co-PI (or the study coordinator) will submit the ISR SAE Form to Pfizer within one business day of the study coordinator's first awareness of the potential SAE.

5.3.2.1. Weekends (Saturday and Sunday): Pfizer requires to report a SAE within one business day; a SAE received on Friday can be reported on Monday (first business day).

5.3.2.2. Any holiday that occurs on a weekday (Monday through Friday) counts as a reporting day i.e., the co-PI (or the study coordinator) will submit the **ISR SAE Form** to Pfizer **within one business day of the study coordinator's first awareness of the suspected SAE.**

**5.3.3.** Absence of co-PI: To meet the one business day reporting timeline, a study coordinator is authorized to submit the ISR SAE Form to Pfizer using the secured protocol.

## **5.4. Follow-up**

**5.4.1.** If a SAE is suspected and a child is still ill (not recovered, not dead), the supervisor will continue monitoring the affected participant's health on a **daily** basis, documenting the findings on form **DCF11-Follow up Report of a Suspected Serious Adverse Event.**

**5.4.2.** **DCF11-Follow up Report of a Suspected Serious Adverse Event** will be filled in, starting on the day following the first filling of DCF10b and continuing until the symptoms have resolved, the child has died or latest 14 days from the first report of the suspected SAE.

**5.4.3.** Once the symptoms have resolved, or the child died or 14 days from the first report of the suspected SAE have passed, the study coordinator will proceed to **DCF12-Suspected Serious Adverse Event Conclusion**.

**5.4.4.** If 14 days have passed and the case is still unresolved, the supervisor will continue monitoring the affected participant's health on a **weekly** basis, documenting the findings on form **DCF11-Follow up Report of a Suspected Serious Adverse Event** until resolution.

## **5.5. Conclusion**

**5.5.1.** The conclusion form is needed for every suspected SAE. The study coordinator will proceed to completing **DCF12-Suspected Serious Adverse Event Conclusion form**:

5.5.1.1. If applicable, immediately after completing form **DCF10b** (see [5.2.2.1](#)).

5.5.1.2. As soon as the case is resolved as indicated on **DCF11-Follow up Report of a Suspected Serious Adverse Event**, or 14 days from the first report of the suspected SAE have passed.

**5.5.2.** The study coordinator will indicate on DCF12-Suspected Serious Adverse Event Conclusion whether the child can continue to receive the study drug.

**5.5.3.** Breaking Study Blinding: The study coordinator will indicate on DCF12-Suspected Serious Adverse Event Conclusion whether it is necessary to break the randomization code for that participant, to know which product the participant was receiving. The data management consulting company (RTI) will provide this information to clinicians taking care of the participant, so that they can take it into account in the medical management and counsel the participant's caregivers about any need to avoid certain drugs in future. The study staff will continue to be blinded to study group assignment in these cases.

**5.5.4.** The study coordinator will also indicate on DCF12-Suspected Serious Adverse Event Conclusion whether the SAE follow-up will continue: if 14 days have passed and the case is still unresolved, the monitoring will continue on a weekly basis (see 5.4.4) until resolved or stabilized as permanent damage (=Recovered with sequelae).

## **5.6. Notification to Pfizer – Conclusion**

**5.6.1.** After the initial reporting of the suspected SAE to Pfizer, and if applicable, information on the outcome of the event after the follow-up will also be transmitted to Pfizer (select 'Follow up Report' on the ISR form) by following procedure described in section 5.3.

## **5.7. Notification to Malian IRB and DSMB**



**5.7.1.** The Malian co-PI (or if unavailable, the study coordinator) will report all suspected SAE to the Malian IRB within 72h of the study coordinator's first awareness of the suspected SAE.

**5.7.2.** The Finnish PI will forward the ISR SAE Form to the Data Safety and Monitoring Board (DSMB), according to the recommendations by the chair of the DSMB.

## 6. Occupational Safety Issues

In a non-epidemic situation, there are no specific occupational safety issues.

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 Hygiene and PPE.

## 7. Quality Assurance / Quality Control

The data collection software will assure all necessary data points are given in the correct format depending on the specific question in the forms. The study coordinator and the Malian co-PI will ensure the accuracy, and timeliness of the data reported to Pfizer.

## 8. Appendices and other related documents

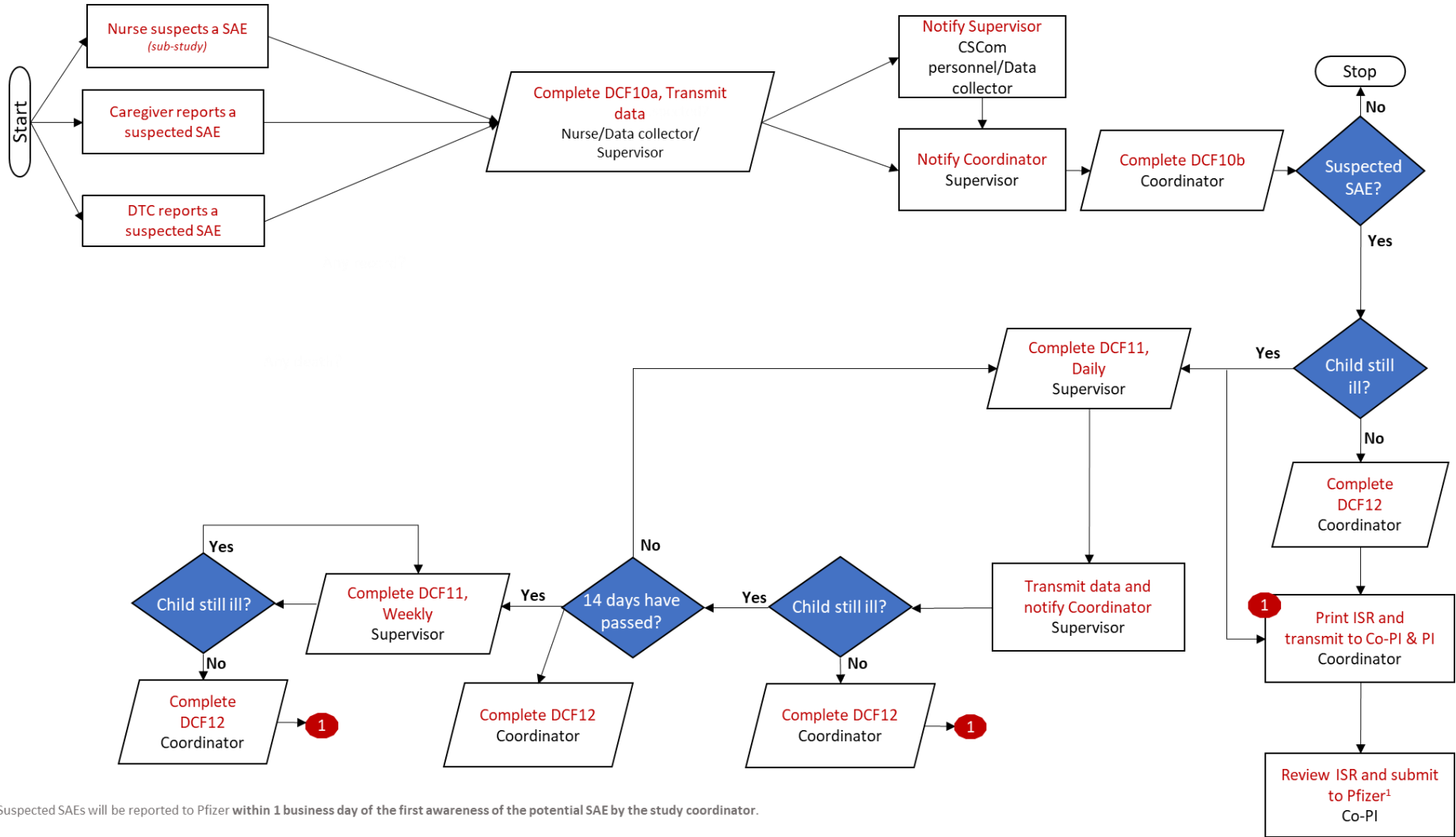
Document number	Document content
Appendix 1	Flowchart on SAE Reporting, Recording and Notification.
Appendix 2	Guidance for using Kiteworks to report an SAE to Pfizer.

## 9. Version history, authors and approvals

Version (date)	Edits to the SOP text (author)
Version 1.0 (2020-08-25)	Authored by Laura Adubra in consultation with LAKANA investigators. Approved by LAKANA PSG.
Version 2.0 (2020-10-07)	Updated instructions on reporting deaths to Pfizer and other regulatory boards (sections 4.2.3 and 4.2.4).  Updated instructions on channel to be used to submit ISR SAE form to Pfizer (section 5.3 and appendix 2).  Authored by Laura Adubra in consultation with LAKANA investigators. Approved by LAKANA PSG.
Version 3.0 (2022-01-18)	Updated instructions on data collection for AEs (section 4.1.3).
Version 4.0 (2023-06-21)	Updated instructions according to:

Version (date)	Edits to the SOP text (author)
	<p>- latest recommendations from the DSMB (i.e., provide clarifications on deaths to be reported as SAEs, and provide definition of inpatient hospitalization)</p> <p>-current version in use of the LAKANA protocol v5.0 (i.e., timing and place of AE active surveillance: MDA 4 at pop-up health facilities in villages)</p> <p>-latest recommendations from Pfizer (e-mail address currently in use to report SAEs, and alternative procedure to submit SAE forms: password-protected emails)</p> <p>Approved by LAKANA PSG.</p>

**Appendix 1: Flowchart on SAE Reporting, Recording and Notification**



<sup>1</sup>Suspected SAEs will be reported to Pfizer within 1 business day of the first awareness of the potential SAE by the study coordinator.

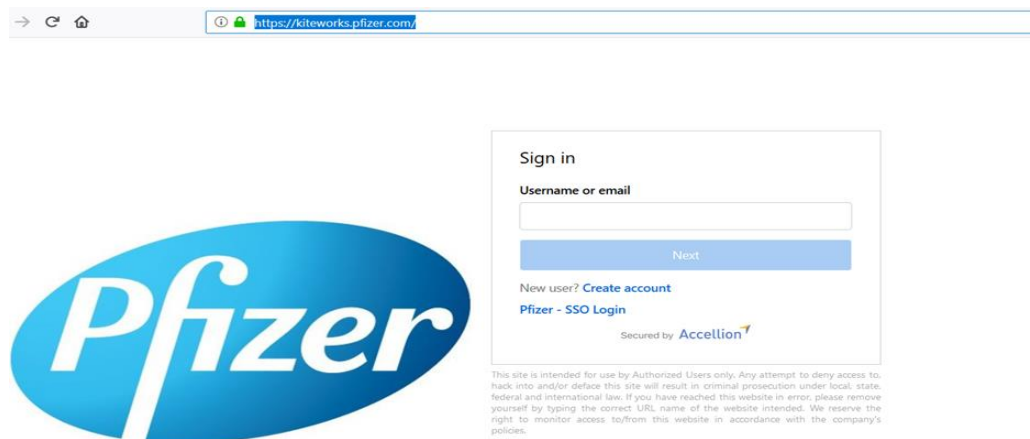
## **Appendix 2 Guidance for using Kiteworks to report an SAE to Pfizer.**

All suspected SAEs will be notified to Pfizer (as described in SOP Proc-02). For this purpose, the Malian co-PI or the study coordinator will submit, for each suspected SAE, an Investigator Sponsored Research (ISR) SAE Form to the Pfizer Morocco and west africa countries DSU at [MAR.AEReporting@pfizer.com](mailto:MAR.AEReporting@pfizer.com)

To submit the ISR SAE Form to Pfizer DSU, the study co-PI or the study coordinator will use the Kiteworks application. Kiteworks is an application that allows files and attachments to be sent to external contacts. The application is available for Pfizer personnel and their external business contacts to transfer files back and forth.

General instructions for logging in Kiteworks and sending an ISR SAE form to Pfizer DSU are listed below:

1. To access Kiteworks, log in on the Kiteworks website: <https://kiteworks.pfizer.com/>.

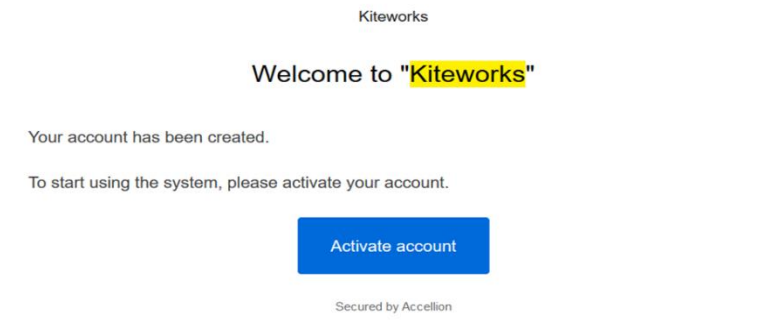


2. If this is your first time, click “create account” and follow the instructions. *Go to section 3 if an account is already available.*

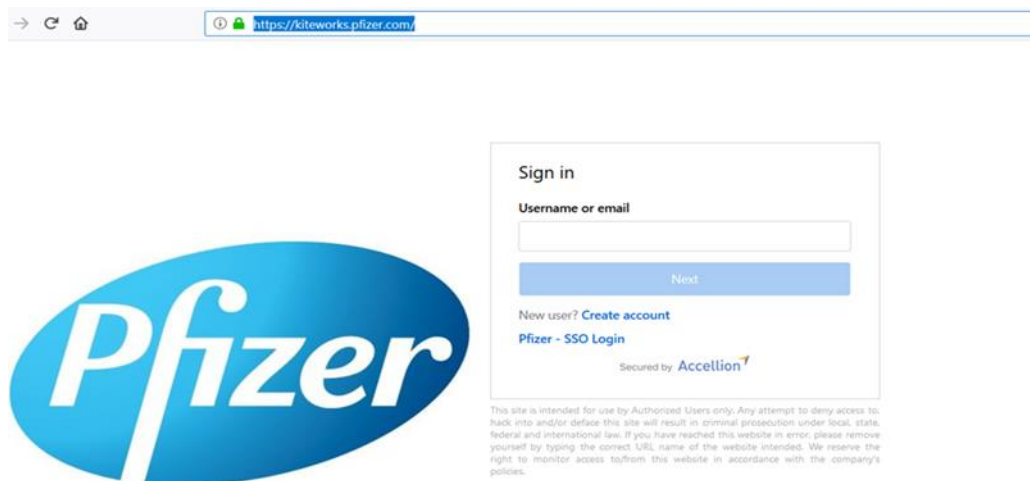
The image shows the 'Create account' form with the following elements:

- Section: Create account
- Text: Already a kiteworks user? [Sign in](#)
- Field: Email
- Field: Password
- Field: Confirm Password
- List of requirements:
  - 1 number
  - 1 uppercase character
  - 8 characters minimum
- Button: Next

2.1. You will receive an e-mail to activate your account, Activate the account.

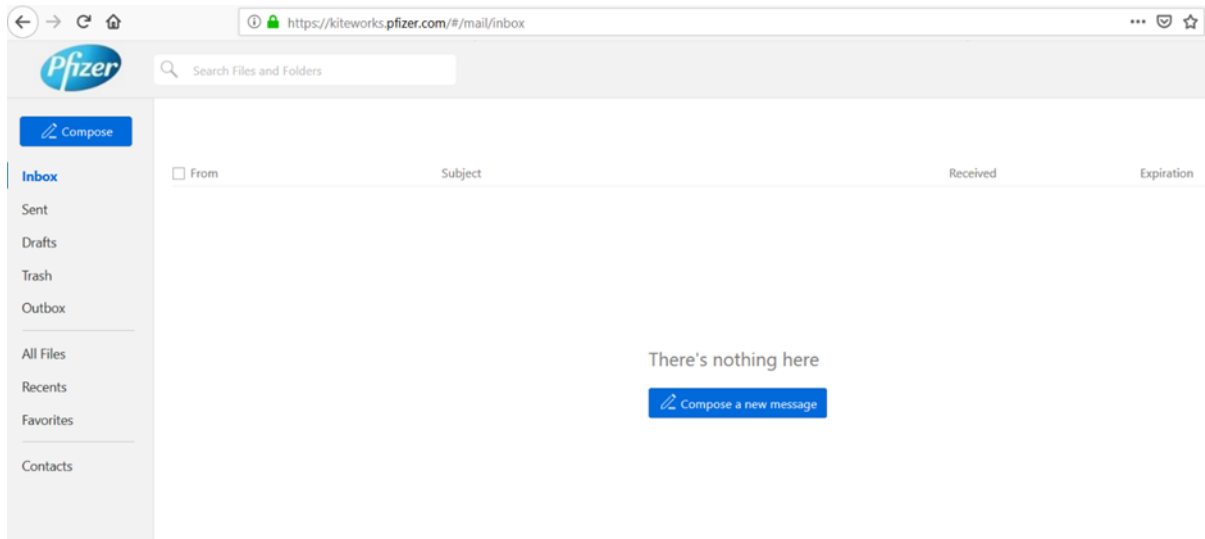


3. Sign in to Kiteworks using your username (e-mail address activated) and your password.

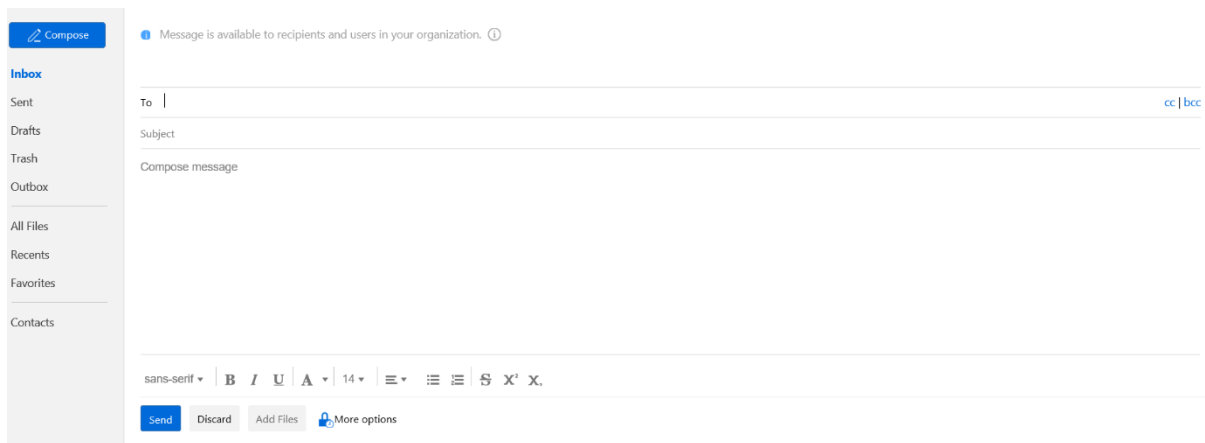


4. From sender's side, using Kiteworks is like using regular email with the exception that it can only be used to send mail to Pfizer addresses.

The recipient of a Kiteworks file will receive an email containing a secure link. The recipient can click the secure link to download the file.



5. To create a new message: click on 'Compose'.



6. Write the message, attach the *ISR SAE form* completed for the suspected SAE you are reporting.

7. Enter the recipient address i.e. DSU address: [MAR.AEReporting@pfizer.com](mailto:MAR.AEReporting@pfizer.com)

8. Click on 'Send' to send the message.