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| **STANDARD OPERATING PROCEDURE for Nigeria PreP Study** |
| **Study Site:**  | **SOPs Number** : DA-401 |
| **Title****INVESTIGATIONAL DRUG MANAGMENT**  |
| **Version Number**:  | **Version Date:**  | **Effective date**:  |
| **Approval name Signature Date**  |

**Annual Review**

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| **Review date**  | **Revision Date**  | **Signature** |
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**Document History**

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| **Version number**  | **Reason for change**  | **Date**  |
| 1.0 | Initial release  | 28th March 2015 |
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**Distribution List**

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1. **Introduction**

The legal status of Investigational product (IP) for human use in clinical study varies from country to country. While in some, these products are manufactured and inspected like “normal” licensed pharmaceutical products, in others they are not covered by legal and regulatory provisions in the area of good manufacturing practice (GMP) inspection, etc. However for the Nigeria PreP study purpose, the WHO guide on GMP is applicable and must be adhered to in the use of IP during the trial.

1. **Objectives**

This standard operating procedure (SOP) describes the processes for the receipt, storage, dispensing, reconciliation, return or authorized destruction and monitoring of the investigational drug (study drug).

1. **Responsibility**
* **Principal Investigator or designee:** Provides directions to the clinical team on the supply, storage, accountability, distribution, reconciliation, donation, return/destruction of IP, develops and distributes study-specific documentation, and acts as liaison with the clinical supplies facility regarding the supply of IP for the study.
* **Clinical Monitor (CM):** Instructs study site staff on, and verifies adherence to, study-specific requirements for correct storage, handling, distribution, donation, return/destruction and accountability of IP. Documents or checks documentation of, IP procedures. Performs reconciliation at the study site and documents any discrepancies. Submits IP documentation for filing in the Central Study File.
1. **Definitions**
* **Investigational Product:** A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use. (ICH – GCP section 1.33 )– in this case is Truvada
* **Investigator's Brochure**: A compilation of the clinical and nonclinical data on the investigational product(s) which is relevant to the study of the investigational product(s) in human participants (see 7. Investigator’s Brochure). (ICH – GCP section 1.36)

**4. Procedures**

**Pre-trial Identification of Sponsor Requirements and Clinical Responsibilities**

The PI or designee determines with the Sponsor, and in accordance with the study Plan, the requirements, responsibilities and approvals for IP related activities including the following:

1. **IP Packaging, Handling, Labelling and Shipping Requirements**

Requirements for packaging and labelling (including expiration date) of IP used in the study, including the following:

* Identifies these requirements by review of the protocol and discussion with the suppliers facility and the sponsor, if appropriate
* Identifies any study-specific, and/or country and local labelling requirements;
* Identifies requirements for translation of labels if need be
* Checks that all labels to be used in the study have been approved in writing
* according to the project-specific procedures
* Checks that the expiration date and batch number are either printed on the label or documented in the Central Study File. If not, requests from sponsor.
* Identifies handling requirements, including precautions required by CM.
* Determines with the sponsor and documents the party who is responsible for storage of bulk IP (clinical supplies facility) and shipment of IP to study site(s);
* Determines with the sponsor which essential documents are required for approval of release of IP to the sites, completes the Investigational *Product Release Form (Appendix 1)*.
* Determines with the sponsor if the site must receive IP prior to the Site Initiation Visit.
1. **Distribution of IP Shipping Information**

The PI or designee provides the following IP shipping information to the clinical supplies facility:

* type of shipment, quantity, and estimated date of arrival based on contractual obligations
* country-specific import/export requirements, if applicable
* investigator site information, as appropriate (for example, name of investigator/pharmacist,
* shipping address, customs/legal requirements)
* requirements for notification of IP shipments to study sites and CM
1. **Documentation of IP Requirements at Study Sites**

The PM or designee develops or obtains from the sponsor study-specific written instructions and/or forms for handling, storage, and accountability of IP at study sites including the following:

* requirements for tracking, shipping, and reporting device malfunctions (if applicable);
* any special dispensing needs required at the study sites for example;
* determines and informs the clinical team how often IP returned by subjects should be checked and reconciled by the CM;
* determines and informs the clinical team how often returned IP is to be retrieved from/destroyed at study sites (or designated local destruction facilities) or donated . The process is authorized by the sponsor in writing. IP related procedures are documented in the Clinical Management Plan.

The PI or designee distributes the IP documentation, including instructions and/or forms, to clinical team members, as appropriate.

1. **CM Responsibilities**

The CM performs the following activities in accordance with the study Plan:

* Obtains study-specific documentation required for written release and shipment of IP to each study site.
* Completes and signs the *Investigational Product Release Form*, obtains authorization from the PM or designee or Regulatory Affairs if applicable and forwards it to the clinical supplies facility.
* Provides study-specific written instructions and forms to investigators/pharmacists for handling, storage and accountability of IP
* If a site requests to use its own forms, the CM checks that they capture the same information required on study-specific forms and informs the PI or designee
* Checks that study-specific requirements can be performed at sites
* Checks the IP on-site before the IP is dispensed to the first Participant , if notified by the PI or designee that this is required
* Records details of receipt of IP in writing and obtains a copy of the signed and dated shipping receipt from the sites for filing in the Central Study File.
* Checks any study-specific storage requirements are being met at the sites, for example, temperature and humidity of the storage facility are appropriately monitored;
* Checks that pharmacy procedures for storage and dispensing is in keep with GMP and GCP

**During the study**

The PI or designee, unless noted otherwise, will perform the following activities in accordance with the study Plan:

1. **Coordination of IP Shipment and Return**

The PI or designee maintains documentation of all IP procedures in the study Plan and distributes updates as appropriate.

For the first shipment of clinical supplies to a clinical site, the *Investigational Product Release Form* or similar form must besubmitted with to the PM or designee to confirm that the site has submitted all requiredregulatory documents and is approved to receive clinical supplies.

The PI or designee checks that site-specific information (names, addresses, and

customs/legal requirements) are kept up-to-date. Coordinates with the sponsor and/or

suppliers the conditions for returning IP (for example, empty containers/packaging, as appropriate), to the clinical supplies facility. Coordination will involve shipping method, completion of required forms, special handling conditions, etc.

Notifies CM of conditions for returning IP.

1. **Coordination of IP Re-Labeling**

The PI or designee:

* obtains written confirmation of any extension of the expiration date for specific batch numbers from the sponsor prior to re-labeling
* Determines with the sponsor who is to attach the replacement labels at the sites
* Co-ordinates with clinical supplies facility the study-specific procedures for relabeling of IP as a result of re-assay and extension of expiration date of the supplies
* Provides written instructions on the re-labeling procedures to the monitors in the form of a Project Instruction, taking local regulations into account
1. **On-Site Monitoring Activities**

The CM performs the following activities in accordance with standard procedures and the study plan:

* Site Monitoring Visit for IP-related activities to be performed at monitoring visits including the following activities, where applicable:
* Performs reconciliation, documents discrepancies, reviews discrepancies with site staff, and obtains documented resolution/explanation of any discrepancies.
* Obtains copies of IP documentation from the investigational site (for example, shipping/receipt records, inventory logs, and return or destruction forms) and submits for filing in Central Study File.
* Periodically checks, during monitoring visits, that IP is within its expiration date(s), and documents in the site visit report that this has been done, including:
* Checks periodically at monitoring visits for any visible indicator of expiration
* Checks correct shipping or storage conditions are being maintained
* Coordinates the re-supply of IP, taking into account the current rate of usage, lead-time required by the suppliers, transit time from the clinical supplies facility to study site and the additional import documentation, as required
* Checks that a limited-access, secure storage area continues to be available, adequate, and locked when not in use.
* Reviews dispensing procedures with pharmacy and/or clinical staff at regular intervals.
* Checks CRF entries and other records relating to IP used or returned by participants against the returned material on-site and documents any discrepancies.
* Checks and count returned IP.
* Completes and/or verifies all information recorded relating to return of the IP to the supplier, and obtains a dated signature from the investigator or an authorized designate. Includes documentation of returns in the return shipment, and submits for filing in the Investigator’s Site File and the Central Study File.
* Participates in re-labelling procedures as instructed by the PI or designee in the study plan.
* Notifies study sites of requirements to quarantine/return expired IP, and re-supply, notify subjects if necessary, or participate in re-labelling of supplies with extended expiration dates, if instructed to do so by the PI or designee.
* Checks and records in the site visit report compliance with IP storage, handling, dispensing, retrieval and accountability.
* Documents outstanding issues and actions in the appropriate site visit report and follow-up letter to the Investigator.

**Site Closure**

1. **Procedures for IP Return and/or Destruction**

The PI or designee determines with the sponsor if IP is to be returned to the supplier, donated to the site HIV treatment clinic or destroyed at the site or local destruction facility.

The PI or designee obtains written authorization from the sponsor if IP is to be donated, or destruction is to occur at the study site, or at a designated local destruction facility and approves destruction of IP in writing.

Appendix A

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| **INVESTIGATIONAL PRODUCT RELEASE FORM** |
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| **Study Title:**  | **Sponsor:** |
| **Principal Investigator:** |
| **Site Name:** |
|  |
| **1. STUDY SITE DOCUMENTS ESSENTIAL FOR IP RELEASE:** |
| **Investigational Product:** |
|  |
|  **All study site documents required for IP release have been obtained, reviewed and** **Approved.**  |
|  |
| **Authorization for IP release:** |
| **Name/Job Title:** |
| **Signature:**  | **Date:** |
| **Name/Job Title:** |
| **Signature:**  | **Date** |
|  |
| **2. INVESTIGATIONAL PRODUCT TO BE SENT TO:** |
| **Shipping Address (Institution, street address, city, state/province, postal code, country):** |
| **Name (first, middle initial, last):** |
| **Telephone Number:**  | **Email address:**:  |
|  |
| **Date Investigational Product needs to be on site** (dd/mmm/yyyy):  |
|  |
| **3. SPECIAL INSTRUCTIONS FOR DELIVERY:** |
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**This SOP has been read and understood by:**

|  |  |  |  |
| --- | --- | --- | --- |
| **Name**  | **Date**  | **Name** | **Date**  |
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