

## **Appendix S1: Operating Procedure for Sample Collection Teams**

### **1. Scope**

This operating procedure details the sample collection procedures for the Post Marketing Quality Surveillance Study of Oxytocin Ampoules (Injection for Solution) in Ethiopia. These procedures should be adhered to by the sampling teams in the collection of all samples from all facilities.

### **2. Objectives of the Study**

The overall objective of the study is to determine the quality of oxytocin ampoules in three regions of Ethiopia by collecting samples and evaluating a number of quality attributes including oxytocin content, microbiological quality and regulatory status.

#### **Specific Objectives**

- To compare the quality of oxytocin ampoules collected from Addis Ababa and the Oromia and Afar regions.
- To assess the quality of oxytocin ampoules at different levels of healthcare facility within those regions
- To assess the quality of oxytocin ampoules within public and private healthcare facilities
- To evaluate the quality of oxytocin ampoules at different points in the public healthcare supply chain between point of entry into Ethiopia and point of use.

### **3. Sample Collection Teams**

Sample collection teams will be provided by MERQ Consultancy and comprise a minimum of two individuals trained in this protocol and sampling collection operating procedure. The sample collection teams will be trained and supervised by the management team at MERQ Consultancy.

#### 4. Selection of Sampling Sites

The study will be conducted in three regions of Ethiopia:

- Addis Ababa
- Oromia
- Afar

As a minimum, samples should be collected from the following facilities in each region:

Addis Ababa:

- 3 Hospitals (Public)
- 3 Health Centres (Public)
- 3 Private Pharmacies
- 3 Private Maternity Clinics
- PFSA Central Store
- PFSA Airport Store

Oromia:

- 3 Hospitals - Urban (Public)
- 3 Health Centres - Urban (Public)
- 3 Hospitals - Rural (Public)
- 3 Health Centres - Rural (Public)
- 3 Private Pharmacies
- 3 Private Maternity Clinics
- PFSA Regional Hub

Afar

- 1 Hospital - Urban (Public)
- 3 Health Centres - Urban (Public)
- 1 Hospitals - Rural (Public)
- 3 Health Centres - Rural (Public)
- 3 Private Pharmacies
- 3 Private Maternity Clinics
- PFSA Regional Hub

Public facilities should be selected in consultation with the selected regional PFSA hubs to identify facilities that are supplied by that hub. It is important that all public healthcare facilities selected must be supplied from the selected regional distribution hub in order that samples come from a single supply chain. Beyond these criteria, all facilities (public and private) should be selected on the basis of likelihood to hold sufficient oxytocin ampoule supplies and accessibility for sample collection. In addition, private facilities should be selected from locations close to selected public facilities to increase collection efficiency.

Alternate sampling sites for all facility groups in each region should be prospectively identified, to be used in the event of sample collection not being possible at the sites originally selected.

Location details and directions for each facility should be recorded to assist sample collection teams in accessing the facility.

## 5. Sampling Technique

Samples from all public facilities (including central stores and distribution hubs) should be collected using an overt sampling methodology, while a mystery shopper approach should be used to collect samples from private facilities

### 5.1 Overt Sampling

Sampling from public facilities should be conducted in an open way supported by the authorisation received from the Federal Ministry of Health (FMoH). A key contact for each facility should be identified and contacted in advance, and informed that the facility has been selected as a sampling site for this study. The key individual should be reassured that the study has received FMoH and FMHACA authorisation and that samples will be replaced with equal numbers of oxytocin ampoules. Once facility participation in the study has been approved by the key individual, a collection date should be agreed. Once a sample has been identified, the collectors should confirm that the sample was supplied from the selected regional PFSA hub. If the sample was acquired from elsewhere (including through private channels) this should be noted on the sample collection form.

### 5.2 Mystery Shopper Sampling

Sampling from private facilities should be conducted covertly where a member of the sample collection team poses as a customer and seeks to purchase the sample from the private vendor. Possible sampling strategies should be agreed in advance such as acting as a researcher or NGO, or purchasing on behalf of an 'out-of-stock' facility.

## 6. Sample Definition

All samples collected should be 1mL ampoules containing 5IU or 10 IU oxytocin solution for injection.

A sample is defined as 25 ampoules from a single batch of product from a given manufacturer. One sample (i.e. 25 ampoules) should be collected from every manufacturer identified at a single facility.

If 25 ampoules from a single batch are not available for sampling, an abbreviated sample of 9 ampoules should be collected.

## 7. Sample Collection and Handling

The sampling team should ensure they have the following items prior to beginning collection at any facility:

- FMoH authorisation letter to conduct study
- EFMHACA list of authorised oxytocin ampoule products
- Cold storage container to maintain refrigerated or cool conditions for collected samples and replacement ampoules
- Sufficient replacement ampoules (10IU/mL oxytocin solution for injection)
- Sample collection forms
- Camera
- Facility details including location and contact details of the key contact (public facilities only)
- Funds to purchase samples (private facilities only)

The following guidance should be used during sample collection:

- Every effort must be made to collect samples in their original packaging.
- When samples cannot be collected in the original packaging, the sample will be collected using ad hoc packaging pre-prepared by the sample collection team.
- For each sample collected, the Team will complete and sign the sample collection form (Appendix 2). For private facilities, this should be done after leaving the sampling site in order to avoid triggering unnecessary suspicion and or questions. Deviations from this operating procedure must be recorded on the sample collection form.
- In order to avoid confusion, each sample will be identified by a unique code number based on Region-Facility Type- Urban/Rural-Public/Private-Sequential Number where:

<u>Region</u>	<u>Facility Type</u>	<u>Urban/Rural</u>	<u>Public/Private</u>	<u>No.</u>
AA = Addis	Hos = Hospital	U = Urban	Pub = Public	01
OR = Oromia	HC = Health Centre	R = Rural	Priv = Private	02
AF = Afar	Pharm = Pharmacy			03
	Hub = Distribution Hub			
	CS = Central Store			
	Arpt = Airport			

Example – the first public hospital in an urban setting in Afar would receive the code AF-Hos-U-Pub-01

- Where possible, a photograph of the sample and packaging should be taken and annotated with the sample code.
- When it is necessary to collect more than one original package in order to obtain the required number of units, all original packaging will be marked with the appropriate sample code number.
- The medicine labels and package leaflets should not be removed or damaged.
- Packages belonging to one sample and the corresponding sample collection form will be kept together (e.g. ampoules/packaging inserted into a dedicated envelope/container marked with the appropriate sample code).
- Care must be taken to protect the samples and their packaging during transportation and ensure samples reach the testing site without any physical or chemical damage.
- The collected samples should be placed into a cold storage container as soon as possible after collection. Samples should be maintained at 2-8°C during transportation back to Addis Ababa where they should be transferred immediately into refrigerated storage. Any period where the samples are exposed outside of the cold chain should be recorded in detail on the sample collection form. Particular attention should be given to the duration of non-refrigerated storage and the temperature to which the sample was exposed.
- Once all samples have been collected key contacts at Monash University and EFMHACA should be informed to arrange transportation to testing sites.

**Appendix S2: Sample Collection Form**

**Oxytocin Injection Ampoule Quality Study**

Region: \_\_\_\_\_

Type of health facility/outlet: \_\_\_\_\_

Setting (urban or rural): \_\_\_\_\_

Sample Code:        -        -        -        -

Name and address of facility: \_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

GPS Coordinates of facility: \_\_\_\_\_

Location from which samples were collected:   Pharmacy                   

  Point of use               

  Other                       

Details: \_\_\_\_\_

\_\_\_\_\_

Name and organisation of people who collect the sample:

1. \_\_\_\_\_

2. \_\_\_\_\_

Manufacturer: \_\_\_\_\_

Product strength:                   5IU    10IU

Batch/lot number: \_\_\_\_\_

Date of manufacture: \_\_\_\_\_ Expiry date: \_\_\_\_\_

Date the batch/sample was received at the location: \_\_\_\_\_ Not known

Number of ampoules collected: 25  9  Other

Details: \_\_\_\_\_

\_\_\_\_\_

Storage conditions of sample at time of collection: \_\_\_\_\_

\_\_\_\_\_

Temp/RH in refrigerator (if appropriate): Temp: \_\_\_\_\_ RH: \_\_\_\_\_

Temp/RH in room of storage: Temp: \_\_\_\_\_ RH: \_\_\_\_\_

Photo taken of packaging: Yes  No

Regulatory status of sample: Market Authorisation   
EFMHACA Waiver   
Not registered   
Not known

Date of collection: \_\_\_\_\_

Signature of persons collecting samples:

1. \_\_\_\_\_

2. \_\_\_\_\_

**Post-Collection Sample Handling**

Details of sample storage conditions following collection (please detail any periods the samples were not maintained in the cold chain):

**Deviations**

Details of deviations from the operating procedure for sample collection should be recorded:

**Table S1: Sample Details and Laboratory Test Results**

Region	Type of Health Facility	Manufacturer	Batch Code	Setting	Oxytocin content (%)	Microbiological Testing		Registration Status at Time of Collection
						Sterility	Endotoxin	
Addis Ababa	Public PFSA	RotexMedica	60532	Urban	105.2	Complies	Complies	Unregistered
Addis Ababa	Public Hospital	RotexMedica	60532	Urban	105.7	Complies	Complies	Unregistered
Addis Ababa	Public Hospital	RotexMedica	60532	Urban	105.5	Complies	Complies	Unregistered
Addis Ababa	Public Hospital	RotexMedica	60532	Urban	106.0	Complies	Complies	Unregistered
Addis Ababa	Public HC	RotexMedica	60127	Urban	104.0	Complies	Complies	Unregistered
Addis Ababa	Public HC	RotexMedica	60532	Urban	106.4	Complies	Complies	Unregistered
Addis Ababa	Public HC	RotexMedica	50158	Urban	105.9	Complies	Complies	Unregistered
Addis Ababa	Private Hospital	RotexMedica	70234	Urban	108.5	Not tested due to insufficient samples		Unregistered
Addis Ababa	Private Hospital	Novartis	S0641	Urban	108.9	Not tested due to insufficient samples		Registered
Addis Ababa	Private MCH Clinic	RotexMedica	60532	Urban	109.0	Complies	Complies	Unregistered
Addis Ababa	Private Pharmacy	RotexMedica	60532	Urban	104.5	Complies	Complies	Unregistered
Addis Ababa	Private Pharmacy	RotexMedica	60126	Urban	101.9	Complies	Complies	Unregistered



Region	Type of Health Facility	Manufacturer	Batch Code	Setting	Oxytocin content (%)	Microbiological Testing		Registration Status at Time of Collection
						Sterility	Endotoxin	
Addis Ababa	Private Pharmacy	Novartis	S0630	Urban	106.0	Complies	Complies	Registered
Oromia	Public PFSA	RotexMedica	60534	Urban	108.7	Complies	Complies	Unregistered
Oromia	Public Hospital	RotexMedica	60127	Urban	95.3	Complies	Complies	Unregistered
Oromia	Public Hospital	RotexMedica	60127	Urban	102.6	Complies	Complies	Unregistered
Oromia	Public Hospital	RotexMedica	60534	Urban	108.6	Complies	Complies	Unregistered
Oromia	Public HC	Biologici Italia	IM1504	Urban	99.9	Complies	Complies	Unregistered
Oromia	Public HC	RotexMedica	60534	Urban	103.9	Complies	Complies	Unregistered
Oromia	Public HC	RotexMedica	60405	Urban	102.1	Complies	Complies	Unregistered
Oromia	Private Hospital	RotexMedica	60127	Urban	106.6	Complies	Complies	Unregistered
Oromia	Private HC	RotexMedica	60405	Urban	100.3	Complies	Complies	Unregistered
Oromia	Private MCH clinic	RotexMedica	60127	Urban	100.9	Complies	Complies	Unregistered
Oromia	Private Pharmacy	RotexMedica	50158	Urban	99.8	Complies	Complies	Unregistered
Oromia	Private Pharmacy	Biologici Italia	IM1511	Urban	101.1	Complies	Complies	Unregistered

Region	Type of Health Facility	Manufacturer	Batch Code	Setting	Oxytocin content (%)	Microbiological Testing		Registration Status at Time of Collection
						Sterility	Endotoxin	
Oromia	Private Pharmacy	RotexMedica	70531	Urban	101.0	Not tested due to insufficient samples		Unregistered
Oromia	Public Hospital	RotexMedica	60127	Rural	102.2	Complies	Complies	Unregistered
Oromia	Public Hospital	RotexMedica	60127	Rural	101.8	Complies	Complies	Unregistered
Oromia	Public Hospital	RotexMedica	60532	Rural	101.2	Complies	Complies	Unregistered
Oromia	Public HC	RotexMedica	60534	Rural	109.4	Complies	Complies	Unregistered
Oromia	Public HC	RotexMedica	60404	Rural	105.7	Complies	Complies	Unregistered
Oromia	Public HC	Novartis	S0601	Rural	102.0	Complies	Complies	Registered
Afar	Public PFSA	RotexMedica	60127	Urban	98.1	Complies	Complies	Unregistered
Afar	Public Hospital	RotexMedica	60127	Urban	98.3	Complies	Complies	Unregistered
Afar	Public Hospital	RotexMedica	60404	Rural	98.6	Complies	Complies	Unregistered
Afar	Public HC	RotexMedica	60532	Urban	100.6	Complies	Complies	Unregistered
Afar	Public HC	RotexMedica	60773	Urban	100.7	Complies	Complies	Unregistered
Afar	Public HC	Biologici Italia	UFN4060 N	Urban	96.5	Complies	Complies	Unregistered
Afar	Public HC	RotexMedica	60773	Rural	101.7	Complies	Complies	Unregistered
Afar	Public HC	RotexMedica	50158	Rural	78.3*	Complies	Complies	Unregistered

Region	Type of Health Facility	Manufacturer	Batch Code	Setting	Oxytocin content (%)	Microbiological Testing		Registration Status at Time of Collection
						Sterility	Endotoxin	
Afar	Public HC	RotexMedica	50158	Rural	78.8*	Complies	Complies	Unregistered
Afar	Public HC	RotexMedica	60773	Rural	101.7	Complies	Complies	Unregistered
Afar	Public HC	RotexMedica	60535	Rural	107.1	Not tested due to insufficient samples		Unregistered
Afar	NGO	Biologici Italia	IM1513	Urban	107.4	Complies	Complies	Unregistered
Afar	Private Pharmacy	RotexMedica	50127	Urban	95.8	Not tested due to insufficient samples		Unregistered

\*Retested to verify result (mean result reported)