ZAMBIA MEDICINES REGULATORY AUTHORITY

# GUIDELINE ON RECALL OF MEDICINES AND ALLIED SUBSTANCES

MARCH, 2023

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## ABBREVIATIONS

ADR – Adverse Drug Reaction

CAPA – Corrective and Preventive Action

LRP – Local Responsible Person

MAH – Marketing Authorisation Holder

NMRA – National Medicines Regulatory Authority

SOPs – Standard Operating Procedures

ZAMRA – Zambia Medicines Regulatory Authority

## DEFINITIONS

**Allied Substances:** Include acaricides, cosmetics, disinfectants, food supplements, feed additives and supplements, medical and surgical sundries, medical devices and condoms.

**Authority:** Means the Zambia Medicines Regulatory Authority provided for under section *3* of the Medicines and Allied Substances Act No. 3 of 2013 of the Laws of Zambia.

**Correction**: Means repair, modification, adjustment, re-labelling, or inspection (including patient monitoring) of a product without its physical removal to some other location.

**Counterfeit**: Unauthorized use of trademark, trade name, other identifying mark, imprint, or device, or any likeness thereof to adulterate, falsely purport, or represent that the product was manufactured or distributed by the identified manufacturer or distributor.

**Distributor:** Means the natural or legal person who imports a medicine or allied substance with a view to being placed on the market.

**Falsified**: Medical and Allied Substances that deliberately/ fraudulently misrepresent their identity, composition or source.

**Local responsible person:** means a person residing in Zambia and appointed in accordance with regulation 17 as provided for in SI 79 of 2019.

**Marketing Authorisation Holder:** Means a person/company in whose name a Marketing Authorisation has been granted and who is responsible for all aspects of the medicine and allied substance, including quality and safety and compliance with conditions of registration.

**Mandatory (non-voluntary) recall:** Is when the Authority requests/orders a product recall due to non-compliance to regulatory requirements.

**Medicine:** Means human medicine, veterinary medicine, medicinal product, herbal medicine or any substance or mixture of substances for human or veterinary use intended to be used or manufactured for use for its therapeutic efficacy or for its pharmacological purpose in the diagnosis, treatment, alleviation, modification or

prevention of disease or abnormal physical or mental state or the symptoms of disease in a person or animal.

**Mock recall:** Routine exercises conducted by manufacturers/distributors and/or other various partners in the supply chain to assess their recall procedures and responsiveness.

**Product:** Includes a medicine and an allied substance

**Product owner**: means a marketing authorisation holder, importer, local responsible person, or manufacturer

**Product Withdrawal:** The total removal of a medicinal product from the market that could be due to an irreversible quality, safety or efficacy concern due to published research findings or non-compliance to current Good Manufacturing Practice (cGMP). The withdrawal or cancellation maybe voluntarily initiated by the MAH or manufacturer or by ZAMRA.

**Quarantine:** Put stock on hold for purposes of destruction or rework or further action.

**Recall strategy**: A planned specific course of action to be taken in conducting a specific recall, which addresses itself to matters such as the depth of recall, need for public warnings, and extent or effectiveness checks for the recall.

**Recall:** A process for withdrawing or removing a medicine and/or allied substance, from the pharmaceutical distribution chain because of defects in the product, complaints of serious adverse reactions to the product. The recall might be initiated by the manufacturer, wholesaler or ZAMRA.

**Voluntary recall:** Is when an establishment requests a product recall after discovery of safety issues, product defects or non-compliance to regulatory requirements.

## 1.0 INTRODUCTION

The Zambia Medicines Regulatory Authority (ZAMRA) is a statutory body established pursuant to the Medicines and Allied Substances Act, No.3 of 2013 of the Laws of Zambia ("the Act"). The Authority is responsible for the regulation and control of medicines and allied substances including regulating and controlling the manufacture, importation, exportation, distribution and sale of medicines and allied substances; establish, maintain and enforce standards relating to the manufacture, importation, exportation, distribution and sale of medicines and allied substances; serve and protect the public interest in all matters relating to the sale of medicines and allied substances among other things.

The Authority is mandated by Section 46 of the Act to direct the recall of medicines and allied substances that do not meet the required standards of quality, safety and efficacy. Section 68 of the Act further mandates the Authority to make guidelines that are necessary for the better implementation of the Act.

In accordance with the foregoing provisions, this guideline is issued to facilitate the recall of medicines and allied substances that do not meet required standards of quality, safety and efficacy and shall apply to both mandatory and voluntary recalls of medicines and allied substances.

### 1.1 Objectives

The objectives of these guidelines are to:

(a) set the procedure for product recall in order to ensure effective removal and disposition from the market of medicines and allied substances that do not meet the required standard of quality, safety and efficacy; and

(b) assist the public, the product manufacturer, importer, distributor or local responsible person or marketing authorisation holder of a medicine or allied substance in handling all aspects of product recall in order to safeguard public health.

The process of recall requires effective collaboration amongst the parties involved in the distribution chain, including manufacturers, importers, distributors, retailers, health facilities, users and consumers. These guidelines therefore, may apply to all these during implementation of a recall.

## 1.2 Scope

These guidelines are applicable to all quality defective product reports and to all reported incidents of safety and efficacy received for all medicines and allied substances. These guidelines shall apply to local responsible persons, marketing authorization holders, distributors, manufacturers, wholesalers, retailers, health facilities, research institutes, healthcare providers, patients and the public. The recall may be voluntary or statutory in nature, where the Authority determines that urgent action is required to protect public or animal health. This guideline provides for a stepwise procedure to be followed when developing a recall strategy and also in recall evaluation at every level in order to achieve compliance within the set time frames.

## 1.3 Classification of Recalls

Recalls are classified based on severity of the quality problem, in accordance with the following system:

**Table 1: Classification of recalls**

| CLASS | DESCRIPTION | EXAMPLES | COMMUNICATION OF RISK |
|---|---|---|---|
| I | For dangerous, defective and potentially life-threatening medicines that could result into serious health risks, adverse | • Wrong Product (label and contents are different products)<br>o Correct product but wrong strength, with serous medical consequences<br>o Microbial contamination of sterile injection or ophthalmic product | • Executed up to wholesale, distributor, retail and consumer level.<br>• Public announcements shall be made |

| | | | |
|---|---|---|---|
| | events or even death. | o Chemical contamination with serious medical consequences<br>o Mix up of some products with more than one container involved<br>o Wrong active ingredient in a multi-component product with serious medical consequences<br>o Lack of effectiveness for a life threating condition | using print and electronic media |
| II | For products that could possibly cause temporary or medically reversible adverse health problems or mistreatment. | • Mislabeling e.g. wrong or missing text or figures<br>o Missing or incorrect information<br>o leaflets or inserts<br>o Microbial contamination of non-injectable, non-ophthalmic sterile product with medical consequences<br>o Chemical/ physical contamination (significant impurities, cross contamination, particulates)<br>o Mix up of products in containers<br>o Non-compliance with specification (e.g. assay, stability, fill/ weight or dissolution)<br>o Insecure closure with serious medical consequences (e.g. cytotoxics, child resistant containers, potent products)<br>o Lack of efficacy/ effectiveness for medical condition that is not life threatening | • Executed up to wholesale and retail levels |
| III | For products that are defective but are unlikely to cause or pose a significant health risk or which do not comply with the requirements | • Faulty packaging e.g. wrong or missing batch number or expiry date<br>• Faulty closure<br>• Contamination- microbial spoilage, dirt or detritus, particulate matter | • Executed up to wholesale level |

| | | | |
|---|---|---|---|
| | of the Act in relation to quality, safety or efficacy. | | |

Class I and Class II recalls are considered to be *Urgent Safety-Related Recalls* and must be reported to the Authority for further evaluation and investigation. Class III recalls are usually considered to be *Minimum Risk Recalls* to public health but shall all the same be reported to the Authority.

The classification of a recall shall be determined by the Authority and each recall shall be treated independently.

For international recalls, the Authority shall consider decisions made by other national Medicines Regulatory Agencies (NMRAs).

### 1.4 Levels of Recall

Recalls shall be catergorised into different levels based on severity of the risk, the channels used for distribution of the medicine or allied substance, and the level to which distribution has taken place.
The table below shows the different levels of recall of medicine and allied substance:

**Table 2: Levels of recall**

| Recall Level | Extent of Communication | Remarks |
|---|---|---|
| A | Recall letter to manufacturer, importer and wholesaler to be initiated at all levels, accompanied by media release sent into general circulation | • *Consumer level*<br>• Designed to reach all levels of the supply chain of medicines and allied substances<br>• *Target*: marketing authorisation holder, manufacturer, local responsible person, wholesaler, distributor, retail outlet, |

| | | |
|---|---|---|
| | (*both print and electronic*) | health facility (public or private), animal health facility, healthcare worker, animal health practitioner, patient, customer and user. |
| B | Recall letter to manufacturer, importer and healthcare worker | • *Retail and user facility level*<br>✓ Designed to reach retailer and user facility level<br>• *Target*:<br>✓ All public and private hospital pharmacies;<br>✓ Retail pharmacies;<br>✓ Clinical investigators and the institutions in which clinical investigations are performed;<br>✓ Medical, dental and other health care practitioners;<br>✓ Nursing homes and other related institutions;<br>• Other retail outlets e.g. medicine shops, supermarkets and health food stores; |
| C | Recall letter to manufacturer, importer and wholesaler | • *Wholesale Level*<br>• Designed to reach wholesale dealers and retailers<br>• *Target*: manufacturer, importer, wholesaler, retail outlets<br>• Wholesaler shall call or issue a notice of recall to a retail outlet to return the product |

### 1.5 Timelines for Effective Recall and Rapid Alert System

The following timelines shall apply to product recalls

**Table 3: Timelines for initiating and completing recall of non-compliant medicine or allied substance**

| Recall Class | Initiation Timeline | Physical Recall Timeline |
|---|---|---|
| Class I | Within 24 Hours | Up to 72 Hours |
| Class II | Within 48 Hours | Up to 14 Days |
| Class III | Within 72 Hours | Up to 30 Days |

## 2.0 RECALL PROCEDURE

The Authority shall recall a batch of a medicine or allied substance that does not meet the set standard of quality, safety and efficacy. Recalls can be of two types, namely Voluntary Recall and Statutory Recall.

### 2.1 Voluntary Recall:

Voluntary recall can be triggered by any incident that affects the quality, safety and efficacy of a batch of a product in question such as:

1. If a batch is found not to comply with the approved regulatory specifications during post marketing surveillance and on-going stability studies.
2. If a batch is found to be defective during investigation of a complaint.
3. If the product failure under investigation has impact on already released batches.
4. Failure of visual inspection of retention samples.
5. Evidence of occurrence of serious safety risks associated with use of the product.

### 2.2 Statutory Recall

Statutory recall shall be triggered by the Authority in the following circumstances:

1. where a medicine or allied substance does not meet the set standard of quality, safety and efficacy.
2. where continued supply of a medicine or allied substance on the market is in violation of the Act or any other relevant Law.
3. where the Authority determines that it is not in public interest that a medicine or allied substance continues to be made available to the public.

## 3.0 STEPS OF RECALL PROCEDURE

The recall procedure is divided into the following steps:

### 3.1 Notification of a product quality problem or defect

The manufacturer, marketing authorisation holder, local responsible person, wholesaler, distributor, retailer, health facility, healthcare worker, animal health facility and animal health practitioners shall be required to report all suspected product quality problems and serious adverse events to the Authority in line with the Pharmacovigilance Guidelines.

### 3.2 Initiation of a Recall

#### 3.2.1 ***Voluntary recall***

When the marketing authorization holder, local responsible person, distributor or manufacturer decides to initiate a voluntary recall of a medicine or allied substance, they shall notify the Authority in writing, providing information as outlined below:

##### 3.2.1.1 Particulars to be provided

a) Name;
b) Telephone number;
c) e-mail address

d) Date of report;
e) Origin of the report (Physical address);
f) Nature of the problem;
g) Number of similar reports received; and
h) Results of tests and other investigations on suspected product or other product samples.
i) Any other relevant information

#### 3.2.1.2 Details of the Product

The following details of the product shall be provided:

a) Name and description of the product, including active ingredients, dosage form, strength, MA number, pack size or type; batch number(s) and expiry date;
b) Manufacturer/distributor's contact telephone number and email address;
c) Date manufactured, date released or imported;
d) Quantity manufactured or imported;
e) Country where product was imported from;
f) Local distribution list; and
g) Distribution list of products exported.

### 3.3 Risk evaluation and proposed recall strategy

The following information shall be provided to evaluate the risk and proposed recall strategy:

a) potential risk to consumer or user;
b) recall strategy proposed by the marketing authorisation holder or manufacturer;
c) proposed recall classification and level.

### 3.3.1 Roles and Responsibilities of Stakeholders

#### 3.3.1.1 The Authority

The Authority may initiate a product recall or guide on recalls initiated by a product owner. Although ZAMRA initiates and guides on the recall, the product owner is responsible for removing the product from the market and providing updates.

#### 3.3.1.2 Manufacturer, Wholesaler, Marketing Authorisation Holder, Local Responsible Person, Importers and Distributors

The Manufacturer, wholesaler, Pharmaceutical retailer, Marketing authorisation holder, local responsible person, Importer and Distributor shall:

a) comply with recalls sanctioned by the Authority;
b) develop and implement Standard Operating Procedures (SOPs) on product recall;
c) notify the Authority of recall initiation;
d) conduct an effective recall in consultation with the Authority;
e) assess the effectiveness of the recall process;
f) submit a detailed report on completion of the recall;
g) maintain a register of recalled products; and
h) dispose recalled products in accordance with guideline on disposal issued by the Authority.

#### 3.3.1.3 Health facility and animal health facility

A Health facility and animal health facility shall:

~~a)~~ comply with the implementation of any recall sanctioned by the Authority;
b) develop and implement Standard Operating Procedures for product recall;
c) submit a report on product quality problems to the Authority;
d) maintain a register of recalled product; and
e) dispose recalled products in accordance with guideline on disposal issued by the Authority

#### 3.3.1.4 Healthcare Professionals

The healthcare professional and animal health practitioners shall:

a) comply with and implement any recall sanctioned by the Authority

b) report product quality problems to the Authority.

#### 3.3.1.5 Consumer, User and the Public

The consumer, user and member of the public shall:

~~a)~~ comply with notice of recall sanctioned by the Authority;

b) return recalled products to a health facility, animal health or retailer facility where applicable; and

c) report product quality problems to their healthcare providers or the Authority.

## 4.0 Assessment of Recall

### 4.1 Recall Strategy

Where there is an impending voluntary recall, the Manufacturers, wholesaler, Pharmaceutical retailer, Marketing authorisation holder, local responsible person, Importers and Distributors shall submit to the Authority a proposed strategy to facilitate implementation of the recall strategy in respect of the particular recall. The recall strategy shall be in line with the Standard Operating Procedure on Recall of Medical Products and the following factors:

a) Description of problem;
b) Number of complaints;
c) distribution networks;
d) recovery procedures; and
e) resources for corrective action.

The recall shall be completed by the date as directed by the Authority. However, in the case of unforeseeable delay, the marketing authorization holder, local responsible person, or distributor shall notify the Authority of factors which may affect the duration of the recall action.

The Authority shall require information for the proposed recall strategy by the Marketing authorization holder, local responsible person, distributor, or manufacturer. The proposed recall strategy shall be agreed upon before

implementation and the agreement shall be reached within 24hrs of submission of Pharmaceutical Product Reporting Form and Recall Notification Form.

In the recall strategy, the applicant should mention the following:

a) indicate the proposed level in the distribution chain to which the recall is extending. If the recall only extends to the wholesale level, the rationale of not recalling to retail level should be explained;
b) in case of consumer level recall, additional information should include location of recall distribution channels for consumers;
c) indicate how the message of recall will be delivered to customers e.g. press release or recall letters etc.;
d) If the Marketing Authorisation Holder, local responsible person, distributor and/or manufacturer has a website, it shall promptly post the recall notification on it as an additional method of recall notification;
e) Report on what the customers have been instructed to do with the recalled product. It is important for the recalling establishment to know the name and title of the recall contact person for each consignee in order to expedite the communication process during the recall;
f) The criteria for returning the affected products must be clearly explained;
g) Provide a proposed disposal plan of the recalled products i.e. how the recalled product will be destroyed, reconditioned or returned to the external or local manufacturer; and
h) The disposal of the recalled product shall be done in accordance with guidelines on disposal of pharmaceutical waste. Suffice to mention that the Manufacturers, wholesaler, Pharmaceutical retailer, Marketing authorisation holder, local responsible person, Importers and Distributors shall inform the Authority and Zambia Environmental Management Agency before product destruction. The proposed method of destruction shall be approved by the Authority who shall witness the destruction. A Certificate of Disposal shall be issued by the Authority after destruction of the product.

## 5.0 COMMUNICATION

### 5.1 Notice of Recall

A notice for a statutory recall shall be issued and implemented in line with Section 46 of the Act. In case of a voluntary recall, the Marketing Authorisation Holder, local responsible person, distributor or manufacturer shall prepare and submit a notice of recall with a factual statement of the reasons for the recall of the product, together with specific details that will allow the product to be easily identified to the Authority for approval before publication. The notice of recall submitted to the Authority shall not contain any material that can be viewed as promotional in nature.

The Authority may also issue a notice of recall in addition to the notice of recall from the Marketing Authorisation Holder, local responsible person, distributor or manufacturer.

For retail level recall, the Marketing Authorization Holder, local responsible person, distributor and/or manufacturer should have confirmation for returning all the stock on hand from the consignees.

If safety to the public is involved and distribution is limited, the MAH, LRP or distributor may contact the clients of the information listed above by telephone and followed by a recall letter. The letter should be retained for a period of not less than three (3) months to ensure that any products still in transit or on its way to retail or hospital is adequately managed and quarantined.

### 5.2 Media Release (Public Warning)

In the case of a recall, where a media release is indicated, the MAH/LRP/distributor and the Authority shall draft the text of the media release with the assistance of expert advice where necessary. In the case of a Class I or customer level recall the text of the media release shall be developed by the MAH/distributor, in consultation with the Authority. The media release should

contain sufficient and relevant detail to uniquely define the product, together with a clear outline of the problem (without causing unnecessary alarm) and must state the appropriate response by the consumer, client or user. A 24-hour access telephone number of the MAH/distributor should be given for further information.

In considering the media release by the marketing authorisation holder, local responsible person or distributor, the Authority shall approve the choice of media with the widest coverage.

### 5.2.1 Content of the media release

The recommended content of a media release shall:

a) be signed by the Responsible Pharmacist or authorised person;
b) have a heading indicating **"Urgent Medicine/Allied Substance Recall"**;
c) indicate the Classification and level of the recall;
d) have the name of product, dosage form, strength, marketing authorisation Number, pack size, batch number(s), expiry date and any other relevant information necessary to allow for absolute identification, where applicable;
e) have a brief description of the nature of the defect;
f) have urgency of the action;
g) have reasons for the action or recall;
h) have an indication of a health risk (this should also state exactly what the product may do if taken, i.e. side-effects);
i) provide specific information on what should be done in respect of the recalled medicine/allied substance. Method of recovery or product collection, which will be used;
j) have a contact telephone number and an email; and
k) have a request to retain the media release in a prominent position for 7 days in case stock is in transit, where applicable.

## 6.0 PROGRESS OF RECALL AND REPORTS

### 6.1 Responsibilities of marketing authorisation holder, local responsible person, Distributors and Manufacturers

The marketing authorisation holder, local responsible person, distributor and manufacturer have the following responsibilities in relation to recall of medicines or allied substances:

a) maintain records and establish procedures which will assist in facilitating recall should such action become necessary;
b) implement the recall in the situation where it is necessary:
c) investigate the cause of the product defect and provide the corrective and prevention actions; and
d) ensuring the safety, quality and efficacy of medicines and allied substances is a prime responsibility of the manufacturer and distributors (e.g., importers). The role of the Authority ZAMRA is to monitor and oversee that the recall process is a success.

### 6.2 Records

The Marketing Authorisation Holder, distributor and manufacturer shall maintain records for all the medicines and allied substances manufactured or distributed by them in accordance with the following:

#### 6.2.1 For manufacturers**:**

A system shall be in operation to record complete and up-to-date histories of all batches of products from the starting materials to the finished products and shall allow for the determination of utilization and disposal of all starting materials and bulk products.

#### 6.2.2 For marketing authorisation holder, local responsible person and distributors**:**

a) Records of all sales or distribution (including professional samples and export to other countries) of medicines or allied substance shall be retained or kept

readily accessible to permit a complete and rapid recall of any batch of a medicine or allied substance.

b) the complete records pertaining to manufacturing and distribution shall be retained for two (2) years after the date of transaction or one year after the expiry date of the batch whichever longer.

c) the MAH, distributor and/or manufacturer shall retain records of problem reports received about each product. Problem reports shall be evaluated by competent personnel and appropriate action taken. The evaluation of each report and the action taken shall be shown in the records. A copy of manufacturing, import or distribution records shall be sent to the Authority when a recall is implemented.

### 6.2.3 Problem Reporting

Where evaluation of a problem report concerning a medicine or allied substance indicates that recall may be necessary, the report shall be submitted to the Authority as soon as possible. Any batch of a formulated medicine or allied substance that has been distributed, or any batch of a starting material that is found not to comply with the approved product specifications shall also be reported if it has been used in a distributed medicine or allied substance.

### 6.2.4 Quarantine and collection points for recalled products

For Class I recall, the marketing authorisation holder, local responsible person, distributor and manufacturer shall notify the public within 24 hours upon the decision of recall and quarantine undistributed stock immediately. This includes telephone advice to quarantine stock pending recall or possible recall followed by recall letters if necessary. The consignees should confirm quantity of stock on hand and have all of them returned. All Class I recalls should be completed within 72 hours as stated in this guideline.

For consumer level recall, the marketing authorisation holder, local responsible person, distributor and manufacturer shall set up sufficient collection points for

the recalled products. Information of location of the recall collection points and their operating hours shall be notified to consumers by effective means.

### 6.2.5 Reimbursement Mechanism

The marketing authorisation holder, manufacturer and distributor shall set up a refund mechanism for the recalled products.

### 6.2.6 Post-recall report

At the end of the period directed by the Authority to complete the recall, or at other agreed times, the marketing authorisation holder, local responsible person, distributor or manufacturer shall provide the Authority with an interim report during the recall process for the monitoring of progress within seven (7) calendar days after initiation of the recall. The interim report shall contain the following information:

a) Initial quantity of stock received;
b) Number of organizations or persons to whom the defective product has been supplied;
c) Date and means of notifying them of the recall;
d) Number of responses received from them;
e) Names of the non-responders;
f) Quantity of stock returned;
g) Quantity of stock that has been off shelves pending return to applicant; and
h) Estimated time frame for the completion of the recall.

A final report containing the following information shall be submitted to the Authority within 14 calendar days after commencing of the recall:

a) Circumstances leading to the recall;
b) Consequent action taken by the applicant or manufacturer;
c) Extent of distribution of the relevant batches in and outside Zambia;

d) Result of the recall i.e. quantity of stock returned, collected, outstanding; quantity of stock used by the consignees; quantity of stock not located and date of recall completion;
e) Confirmation that the retailers have returned all the recalled product to the marketing authorisation holder, local responsible person, or manufacturer and the customers have received the recall letter; and
f) Method of destruction or disposal of the recalled products.

The marketing authorisation holder, local responsible person, distributor or manufacturer shall report to the Authority with relevant explanation and obtain its approval if the final report cannot be submitted within 14 calendar days after commencing of the recall. After completion of the recall, a report on investigation results on the problem and the action proposed to be implemented in future to prevent a recurrence of the problem should be submitted to the Authority in a timely manner, not more than 30 calendar days after the recall.

## 7.0 EVALUATION OF THE RECALL

The evaluation consists of a check on the effectiveness of the recall and an investigation of the reason for the recall as well as the remedial action taken to prevent a recurrence of the problem.

### 7.1 Check on the Effectiveness of Recall Action

It is the marketing authorisation holder, local responsible person, distributor or manufacturer's responsibility to ensure that the recall is effective. Recall records may be inspected and in some cases the Authority may contact a percentage of customers in the distribution list as a means of assuring that the marketing authorisation holder, local responsible person, distributor or manufacturer is carrying out its recall responsibilities (see Customer Reply Form in appendix III). If the Authority finds the recall to be ineffective, the marketing authorisation

holder, local responsible person, distributor or manufacturer shall be asked to take appropriate steps, including re-issuing recall letters.

### 7.2 Investigation of the Reasons for Recall and Initiation of Remedial Action

On completion of a recall, the marketing authorisation holder, local responsible person and manufacturer shall provide a report of the investigation on the problem and details of the remedial action proposed to prevent a recurrence of the problem which gave rise to the recall. Where the nature of the problem and appropriate remedial action is not apparent, investigation and in some cases current Good Manufacturing Practice (cGMP) inspections may be necessary.

Where a recall is initiated following a report submitted by a party from external regulatory authorities, the report is to be provided with an outline of the results of investigation and a summary of the recall.

### 7.3 Mock Recall

Mock recall shall be carried out for at least one batch of any product, dispatched for sale where maximum distributors are involved, to test the effectiveness of the proposed procedures in the standard operating procedures. Effectiveness of recall procedure can also be checked by “evaluation of an actual recall”.

Mock Recall shall be performed at least once every three years based on the longest distribution chain and whenever there is a change in the distributor or marketing company.

Records of such mock recall shall be maintained by the person responsible for recalls at the company.

## 8.0 REINSTATEMENT OF SUPPLY

The quality of the products shall conform to specific requirements including finished product specifications before resuming the supply to the public. The marketing authorisation holder, local responsible person, and manufacturer must seek approval from the Authority for reinstatement of the medicine or allied substance previously withdrawn.

### 8.1 Implementation of Remedial Action

The marketing authorisation holder, local responsible person, distributor or manufacturer shall identify the root cause of the problem and implement the corrective action accordingly. Furthermore, preventive action shall be imposed to prevent recurrence of the problem in the future. In some cases, adequate time is required for research and product development to reformulate or change the packaging or to exclude or reduce impurities and degradation products.

### 8.2 Submission of Analytical Report

After implementing the remedial action, subsequent manufacturing or importation of the new batch of the product, the marketing authorisation holder, local responsible person, or manufacturer shall submit analytical report(s) of the new batch tested by external ISO accredited laboratory or WHO prequalified laboratory to the Authority as a proof of product quality if applicable. If the independent laboratory does not have the capacity in terms of equipment to analyze the product e.g. analysis of vaccines or large molecular weight medicines, the manufacturer can perform the analysis and submit the results to the Authority for verification. If the Authority is concerned with the quality of the manufacture, GMP inspection of the site could be conducted. The submitted report(s) will be evaluated by the Authority that will inform the marketing authorisation holder, local responsible person, or manufacturer whether the submitted reports are satisfactory.

### 8.3 Verification of Corrective Action and Preventive Action (CAPA)

When the Authority is satisfied by the submitted reports, samples of the first batch of the product (either being manufactured by the local manufacturer or being imported) will be collected for examination by the Authority before the medicine or allied substance can be distributed. After the Authority has approved the distribution of the product, samples from the next consecutive two batches should be submitted for analysis as part of the verification process if applicable. The cost for analysis shall be borne by the marketing authorisation holder, local responsible person, or manufacturer. Where necessary a third-party independent analysis maybe required in exceptional cases at the cost of

the manufacturer or marketing authorisation holder after approval by the Authority.

## 9.0 PENALTIES

Where there is non-adherence to these guidelines, the Authority shall institute regulatory action and prosecution in accordance with Section 46 (4) of the Medicines and Allied Substances Act No. 3 of 2013 of the Laws of Zambia.

## 10. SUPPORTING RESOURCES

Good Distribution Practices Guideline. Zambia Medicines Regulatory Authority. 3rd August, 2017.

Guidelines for Good Storage Practices, Good Distribution Practice, Pharmaceutical Product Recall. Food, Medicine and Healthcare Administration and Control Authority of Ethiopia (EFMHACA). 1st Edition, September, 2015. Addis Ababa, Ethiopia.

Guidelines for Product Recall. Food and Drugs Authority, Ghana: FDA/DRI/DMS/GL-PRL/2019/05.

## Appendix I: Adverse Drug Reaction, Medication Error & Product Quality Problem Reporting Form

ZAMRA/NPVU/FORM/0001 version 00

**ADVERSE DRUG REACTION, MEDICATION ERROR AND PRODUCT QUALITY PROBLEM REPORTING FORM**

*(Identities of reporter and patient will remain strictly confidential)*

**NATIONAL PHARMACOVIGILANCE UNIT (NPVU)**

The Director General
The Zambia Medicines Regulatory Authority
Plot No. 6903, Tuleteka Rd, Off Makishi Rd,
P.O. Box 31890, Lusaka, Zambia.

Telephone: +260211220429
Telefax: +260211238458
Email: pharmacy@zamra.co.zm

**PATIENT INFORMATION**

Patient initials: ..... File No. ..... Age: ..... Weight (kg): .....

Sex: Male ☐ Female ☐ Date of birth: ..... /..... /..... Height (cm): .....

**DETAILS OF ADVERSE DRUG REACTION OR PRODUCT QUALITY PROBLEM**

I am reporting on: 1) an Adverse Drug Reaction ☐ Date of onset of reaction: ..... /..... /.....

2) a Product Quality Problem ☐ Category: medicine ☐ medical device ☐

Description of Adverse Drug Reaction or Product Quality Problem: .....

.....

.....

**1. MEDICINES/ VACCINES/ MEDICAL DEVICES:** *(✓) Tick against the **suspected** medicine/ vaccine*
Indicate all medicines the patient is taking

| (✓) | Trade/ Generic Name & Batch Number | Dosage & dosing frequency | Route of administration | Start date (dd/mm/yy) | Stop date (dd/mm/yy) | Reasons for use |
|---|---|---|---|---|---|---|
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |

**ADVERSE DRUG REACTION OUTCOME:** ***(Tick all that apply)***

Outcome: ☐ Death ☐ Life threatening ☐ Disability ☐ Hospitalization ☐ Congenital abnormality

☐ Other *(specify):* .....

Recovered: ☐ Yes ☐ No If YES, date of recovery: ..... /..... /.....

Additional information *(e.g. Relevant medical history, medicines taken in the last 28 days, allergies, previous exposure, baseline test results/ lab data)*..... .....

.....

**2. PRODUCT QUALITY PROBLEM**

| Trade Name | Batch Number | Registration Number | Dosage Form & Strength | Expiry Date (mm/yyyy) | Size/ Type of container |
|---|---|---|---|---|---|
| | | | | | |

Product sample(s) have been submitted for evaluation: ☐ Yes ☐ No Number of submitted samples: ☐

**DETAILS OF REPORTER**

Name: ..... Profession: ..... Signature: ..... Date (dd/mm/yyyy):.....

Contact address: ..... Phone: ..... Email: .....

## Appendix II: Pharmaceutical Product Reporting Form (Part I) And Recall Notification Form (Part II)

**Note:**

Part I of this form should be used to report a problem with medicines and allied substances in quality, safety or efficacy, which are thought to have arisen during their manufacture, storage, or handling. Problems of this nature may require laboratory investigation by ZAMRA.

Part II of this form should be completed when a decision of recall is established.

When the reported problem may lead to a Class I or II recall, it should be reported to the Authority by telephone within 24 hours, and followed by email or letter of Part I of this form.

If a Class I or II recall is required, parts I and II of this form should be reported to the Authority immediately by telephone and followed by email or letter.

The manufacturer, marketing authorisation holder, local responsible person, distributor or importer should submit the available information to the Authority as soon as the recall decision is made, rather than waiting until ALL applicable information in part II is this form available.

For a problem that may lead to a Class III recall, Part I of this form should be reported to the Authority by letter or email within 72 hours.

If Class III recall is required, Parts I and II of this form should be submitted by letter or email to the Authority.

Contact information for the Authority:

**The Director General**
**Zambia Medicines Regulatory Authority**
**Plot No. 2350/M Off Kenneth Kaunda International Airport**
**PO Box 31890**
**Lusaka, Zambia**
**Tel: +260 211 432 350 / 432 351**
**Email: pharmacy@zamra.co.zm**

Use a separate form for each pharmaceutical product reported.

**Pharmaceutical Product Problem Report Form (Part I)**

| **DETAILS OF THE PROBLEM** | |
|---|---|
| Reporting company: | |
| Name of contact person: | Position: |
| Name of the organisation | |
| Address: | |
| Email: | |
| Telephone (office): | Mobile: |
| Pharmaceutical product problem occurred in Zambia? If not, location of the problem: | |
| Nature of the problem: | |
| Date of complaint received: | |
| Source of complaint | Patient □ customer □ retailer □ self-inspection □ |
| | Other (specify) |
| Number of similar reports received: | |
| Description of the problem (use separate sheet if this space is not enough) | |
| Results of tests/Investigation on the suspect product or other samples | |
| Has the manufacturer or distributor been contacted? Yes □ No □ (If yes, please provide company names) | |

| |
|---|
| Other relevant information (Attach photo, package insert, and press release of any overseas authority of the product if any) |

| **DETAILS OF THE PRODUCT** | | | |
|---|---|---|---|
| Name of the product (on marketing authorisation certificate) | | ZAMRA MA Number: | |
| Active ingredient and strength: | | | |
| Indications (Attach additional sheet if this space is not enough): | | | |
| Dosage form: | | Pack size: | |
| Batch number: | | Expiry date: | |
| Distribution of products: | Wholesale □ | Hospitals □ | Health centers □ |
| | Pharmacies □ | Drug stores □ | Health shops □ |
| | Clinics □ | Others (specify) | |
| **Manufacturer** | | | |
| Name: | | | |
| Address: | | | |
| Tel (office): | Email: | Manufacture date: | |
| Batch size: | Quantities of batches manufactures: | | |
| Date and quantity released: | | Quantity on hold: | |
| Quantity distributed: | | Local: | |
| | | Overseas: | |
| **Importer** | | | |
| Name: | | | |
| Address: | | | |
| Tel (office): | Email: | Import date: | |
| Quantity of batch imported: | Quantity on hold: | | |
| Date and quantity released | | | |
| | | Local: | |

<table>
<tr><td colspan="2">Quantity distributed:</td><td>Re-exported:</td></tr>
<tr><td colspan="3">Local distributor (please attach distribution list)</td></tr>
<tr><td colspan="3">No. of local distributors:</td></tr>
<tr><td colspan="3">Name:</td></tr>
<tr><td colspan="3">Address:</td></tr>
<tr><td colspan="2" rowspan="2">Contact person:</td><td>Tel (office):</td></tr>
<tr><td>Tel (mobile):</td></tr>
<tr><td colspan="2">Quantity on hold:</td><td>Quantity distributed:</td></tr>
<tr><td colspan="3">Exporter</td></tr>
<tr><td colspan="3">Has the product been exported? YES □ NO □<br>If yes, specify the country/countries:</td></tr>
</table>

Name of Reporter …… Position ……

Contact Number …… Date ……

Signature of the reporter ……

**Recall Notification Form (Part II)**

<table>
<tr><th colspan="3">RISK ASSESSMENT</th></tr>
<tr><td colspan="3">Types of Hazards: Quality □ Safety □ Efficacy □<br>Other □ (specify)</td></tr>
<tr><td colspan="3">Evaluation of hazards to users (i.e., effect on users, possibility of occurrence) (Attach expert advice where applicable)</td></tr>
<tr><td colspan="3">Proposed recall classification: Class I □ Class II □ Class III □</td></tr>
<tr><td colspan="3">Proposed action (with agreement of ZAMRA)</td></tr>
<tr><td colspan="2">Recall start date:</td><td>Proposed recall end date:</td></tr>
<tr><td colspan="3">Hotline(s) for inquiries:</td></tr>
<tr><td>Hotline(s) hours of operation:</td><td>Mon-Fri:</td><td>Sat, Sun, public holiday:</td></tr>
<tr><td rowspan="2" colspan="2">Person responsible for recall:</td><td>Tel (Office):</td></tr>
<tr><td>Tel (Mobile):</td></tr>
<tr><td colspan="3">Proposed level of recall: Wholesale □ Retail □ Consumer □</td></tr>
<tr><td colspan="3">Locations of recall spots (Customer level recall only):</td></tr>
<tr><td colspan="3">Means of refund at recall spots: Cash □ Replacement □<br>Other □ (specify)</td></tr>
<tr><td colspan="3">Proposed recall strategy (use separate sheet if this space is not enough)</td></tr>
</table>

Name of Reporter …… Position ……

Contact Number …… Date ……

Signature of the reporter ……

## Appendix III: Customer Reply Form

| | |
|---|---|
| To | |
| Attention | |
| Email | |
| Postal Address | |
| Subject | |
| From | |
| Contact Person | |
| Telephone (office) | |
| Email | |

We **DO** □ **DO NOT** □ have stock that is subject to this recall.

We have reported and returned all the stock on hand to ……
(Supplier)

Stock Received:

| **Batch No.** | **Quantity** |
|---|---|
| | |
| | |
| | |

Unused stock subject to recall (currently in quarantine)

| **Batch No.** | **Quantity** |
|---|---|
| | |
| | |
| | |

Any other relevant details:
……
……
……

I declare that the information provided by me in this reply form is complete and true to the best of my knowledge.

Signature …… Date ……

## Appendix IV: Post Recall Report Form (Final Report)

| DETAILS OF RECALLED PRODUCT | |
|---|---|
| Product name: | Marketing Authorisation No.: |
| Active ingredient and strength: | |
| Dosage form: | Package size: |
| Batch No.: | Expiry date: |
| Reason for recall: | |
| Extent of distribution: | |
| Imported/manufactured quantity: | |
| Quantity distributed in Zambia: | No. of consignees: |
| Quantity exported: | Countries: |
| Action taken by the product owner (i.e., MAH, LRP, importer, distributor etc.) | |
| Result of recall: | |
| Returned quantity: | Outstanding quantity: |
| Used or sold quantity by the consignees: | |
| Quantity of stock not located: | |
| No. of recall reply forms received from consignees and all stock returned/reported: | |
| Disposal plan: Destroy □ Return to overseas manufacturer □ Other □ (Specify) | |
| Details of disposal method: | |

Name of reporter …… Position ……

Contact Number …… Date ……

Signature of the reporter ……

## Appendix V: Document Related to Submission of Analytical Report

### Accredited Test

The laboratory performing the tests should obtain accreditation on the specific test method in accordance with the international standards, e.g., ISO 17025. The Licensee shall submit the raw data and quality control data for the tested samples to substantiate the validity of test results. These data could facilitate the evaluation of the test result by the EFMHACA laboratory.

### Non-Accredited Test

In case accreditation of the specific test could not be arranged, the analytical report might be considered acceptable if the laboratory has obtained appropriate accreditation in the area of pharmaceuticals or pharmaceutical products, and be able to provide necessary documentation to prove its competence in respect to its quality control and technical aspects in performance of the specific chemical tests.

Basically, the information should include, but is not limited to, the following:

- Detailed method (including standard preparation procedure, sample preparation procedure, instrument parameters, and quality control procedure);
- Raw data and quality control data for all tested samples shown in the report (including chromatograms, mass spectra and calculation);
- Validation summary for the method used (including method linearity, limit of detection, limit of quantitation, method bias, precision, and measurement uncertainty);
- Reference material used and purity verification summary; and
- Relevant proficiency test participation.