Medicines Control Authority of Zimbabwe

MCAZ/LED/GL-15

GUIDELINES FOR THE NOTIFICATION OF MEDICINAL PRODUCT PROBLEM OR DEFECT AND RECALL PROCEDURE IN ZIMBABWE

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Medicines Control authority of Zimbabwe

106 Baines Avenue

P O Box 10559

Harare

Email: mcaz@mcaz.co.zw

Website: www.mcaz.co.zw

Reviewed by:	Signature	20/4/2023 Date
Checked by HoD/HoU:	pp Signature	21/4/2023 Date
Approved by QM:	Signature	25/4/2023 Date
Authorised by Director General:	Signature	25/4/2023 Date

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1.0 APPLICATION

These guidelines apply to all persons legal or real, that deal in the storage and distribution of medicinal products from the manufacturer of medicinal products to the person dispensing or providing medicines directly to the patient. This includes all parties involved in different stages of the supply chain of medical products; manufacturers and wholesalers, as well as brokers, suppliers, distributors, logistics providers, traders, transport companies and forwarding agents and their employees.

2.0 PURPOSE

The Medicines Control Authority of Zimbabwe Medicines Products Recall Guidelines are intended to ensure that in the event of a necessary recall, the recall operations are effectively and efficiently carried out by the manufacturer, importer, distributor or certificate holder of pharmaceutical product (hereafter known as the applicant) in order to safeguard public health.

3.0 BACKGROUND / INTRODUCTION

Medicines, vaccines or medical device products that are suspected of being potentially harmful to users due to their defective quality, safety or efficacy, they may be subjected to a recall and all related information must be reported to the Medicines Control Authority of Zimbabwe (MCAZ).

The role of the MCAZ in a recall is to protect public and animal health by ensuring that accessible medicines including vaccines, allied substances and medical devices are safe, effective and of good quality through enforcement of adherence to standards by manufacturers, distributors, pharmacies, hospitals and clinics. The MCAZ also assesses the nature of product defect and the adequacy of the recall of the product and to monitor the progress and effectiveness of the recall. The MCAZ may alert the public of the product problem and instruct the applicant to recall and dispose of the product according to the nature of the product defect and/or recall. Each applicant, manufacture or wholesaler is supposed to advise MCAZ of the names, after hours and telephone numbers of two persons who have authority and qualifications to discuss, and if necessary implement a recall.

4.0 DEFINITIONS

4.1 Applicant: The person or entity by, or on whose behalf, an application for registration is made, in terms of the Medicines and Allied Substances Control Act (MASCA) Chapter 15:03 Section 2.

4.2 Medicine: Any substance, or mixture of substances manufactured, sold, supplied or offered for sale or supply for use in:

i. the diagnosis, treatment, mitigation, alleviation or prevention of disease or its symptoms; or

ii. the diagnosis, treatment, mitigation, alleviation of any abnormal physical or physiologicalstate or its symptoms; or

iii. altering, modifying, correcting or restoring any organic function in human beings or in animals. **Please note** that vaccines and biologicals are included under the MASCA Chapter 15:03 definition of a medicine

4.3 Product defect: in this context can be a Defective, Substandard and Falsified Medical Product.

4.4 Substandard medical products *also referred to as "out of specification"*: are authorized medical products that fail to meet either their quality standards or specifications, or both.

4.5 Falsified medical products: are products that deliberately or fraudulently misrepresent their identity, composition or source.

4.6 Recall: A process for withdrawing or removing a medicine, vaccine and/or medical device product from the pharmaceutical distribution chain because of defects in the product, complaints of serious adverse reactions to the product and/ or concerns that the product is or may be substandard or falsified. The recall might be initiated by the manufacturer, wholesale dealer applicant or the MCAZ.

4.7 Withdrawal or Cancellation of Registration and/or Withdrawal of a listed product: 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 Practices (cGMP). The withdrawal or cancellation maybe voluntarily initiated by the applicant or manufacturer or by the MCAZ.

4.8 Defect classification: Recalls are classified with regard to the relative health hazard associated with the use of or exposure to the recalled product. There are three possible classifications:

i. **Class I:** Defects are potentially life threatening

ii. **Class II:** Defects could cause illnesses or mistreatment, but are not Class I.

iii. **Class III:** Defects may not pose a significant hazard to health, but withdrawal may be initiated for other reasons.

4.9 Depth of recall: level within the distribution channel from which a product is recalled, i.e. wholesale, retail, user/consumer.

4.10 Batch Recall: the action of withdrawing a batch from the distribution chain and users. A batch recall may be partial, in that the batch is only withdrawn from selected distributors or users.

5.0 GUIDELINES

RECEIPT OF MEDICINAL PRODUCT PROBLEM REPORT

A Medicine, Vaccine or Medical Device Product Problem/ Defect Report Form (LEF 63), *Attachment I* is used to report medicines and/or vaccine/medical device problems to the MCAZ. Upon receipt of the product defect problem the Authority shall determine whether the product is substandard or falsified. If the product is substandard, the recall procedure shall be followed as in section 5.1. If the product is falsified, a risk assessment shall be done to determine the severity of the product problem. An investigation shall be carried out in conjuction with the Zimbabwe Republic Police, Criminal Investigation Department Drugs and Narcotics, within 24 hours for critical products and 48hours for non-critical products. All the batches of the falsified medical product or medical devices, depending on the quantities shall either be confiscated and quarantined at MCAZ or quarantined at site whilst investigations are pending finalization. Once investigations are done the products shall be disposed of at a designated destruction site and a certificate of destruction shall be issued.

5.1 RECALL PROCEDURE

The procedure is divided into five stages, which are set out below, with a reference to the Section in which detailed information is given,

5.1.1 Information Required for Assessment of Recall

Information on product, problem and distribution is required, see Recall Notification Form (LEF 62) *Attachment II.*

5.1.2 Assessment of Recall

The classification, level and strategy of recall are determined depending on the potential hazard of the defective product and the extent of product distribution. See Product Defects Risk Assessment Form (LEF 86), *Attachment VI.*

5.1.3 Recall

Letters and press release (if required) are dispatched to relevant firms for notifying on the recall. See Recall Reply Form (LEF 61), *Attachment III.*

5.1.4 Progress of Recall and Report

Progress reports and final report are submitted to the MCAZ. See Final Report Form (LEF 60), *Attachment IV.*

5.1.5 Evaluation of the Recall

The effectiveness of the recall is monitored by the MCAZ, and a letter is written to the recall initiator either closing the recall or instructing the initiator to redo the recall.

5.2 NOTIFICATION OF A MEDICINAL PRODUCT PROBLEM AND /OR DEFECT

5.2.1 Recall might be initiated as a result of reports or complaints on quality, safety or efficacy on a medicine, vaccine or medical device product referred to the applicant from a variety of sources. The reports or complaints may be referred by manufacturers, wholesalers, retailers, hospital pharmacies, research institutes, medical practitioners, dentists, patients and/or the public.

5.2.2 Recall might also be initiated as a result of analysis and testing of samples of medicinal products by the manufacturers and MCAZ for batch samples that do not meet specifications such as assay, impurities etc. Recall of medicine and/or vaccine/medical device products manufactured outside Zimbabwe might be initiated by the local or external health authorities, or from information received directly from such authorities including National Regulatory Agencies. (NRAs).

5.2.3 Certain information is essential to permit the assessment of the validity of the report of quality defects, safety or efficacy problem with medicines and/or vaccine/medical device products, the potential danger to public or consumers and the action appropriate to the situation. A Medicine, Vaccine or Medical Device Product Problem/ Defect Report Form (LEF 63) is used to report medicines and/or vaccine/medical device problems to the MCAZ.

5.2.4 Serious problems which may lead to recall of Class I or Class II (refer to recall classification under Section 3) must be reported to the MCAZ within 24 hours after receipt of the complaint or report of the investigation. The Medicine, Vaccine or Medical Device Product Problem/ Defect Report Form (LEF 63) together with opinions on toxicological or therapeutic hazards and the action proposed by the NRAs (if any) should be submitted to the MCAZ.

5.2.5 For less serious problems which would result in a Class III recall, the Medicine, Vaccine or Medical Device Product Problem/ Defect Report Form (LEF 63) should be sent to the MCAZ no later than 72 hours after receipt of complaint or report of a problem.

5.2.6 It should be noted that the applicant has to send the Medicine, Vaccine or Medical Device Product Problem/ Defect Report Form (LEF 63) to the MCAZ prior to their decision to recall the product.

5.2.7 In case of a potential significant health hazard to patients during weekends or public holidays the applicant may within 24 hours initiate action which could include precautionary measures to block or quarantine stock prior to the initiation of the recall.

5.2.8 When the need for recall has been established, additional information is required so that an appropriate recall strategy may be devised.

5.3 INITIATION OF RECALL/ INFORMATION REQUIRED FOR ASSESSMENT OF RECALL

When the MCAZ and/or applicant and manufacturer decides to initiate a recall on a medicine and/or vaccine/medical device, it is required to notify the recall situations with the Recall Notification Form (LEF 62) including information outlined below to the MCAZ immediately after the decision to make a recall is made. The MCAZ will also inform other key stakeholders of the intent to recall the product such as the Directorate Pharmacy Services - MoHCC. The information required may include:

5.3.1 Details of the Problem

i. name, telephone and e-mail address of the person reporting the problem;
ii. date of report;
iii. physical location of the problem;
iv. nature of the problem;
v. number of similar report received;
vi. results of tests and other investigations on suspected product or other product samples.

5.3.2 Details of the Product

i. name of the product and description including active ingredients, dosage form, strength, registration number, pack size or type; batch number(s) and expiry date;
ii. manufacturer/ distributors contact telephone and email address;
iii. date manufactured, date released or imported to Zimbabwe
iv. quantity of the batch, date and amount manufactured, released or imported to Zimbabwe;
v. local distribution list;
vi. distribution list of product exported outside Zimbabwe; -

5.3.3 Health hazard evaluation and proposed action

i. type of hazard, and evaluation of health hazard to user;
ii. action proposed by the applicant or manufacturer;
iii. proposed recall classification and level; and
iv. availability of alternative product.
v. all affected batches of the product should be quarantined under safe storage conditions

5.4 ASSESSMENT OF RECALL

5.4.1 Recall Strategy

Each recall is a unique exercise. There are a number of factors common to all recalls that need to be considered in tailoring an appropriate recall strategy. These include the nature of the deficiency in the product, the incidence of complaints, public safety, distribution networks, recovery procedures, resources for corrective action and availability of alternative products.In determining the recall strategy, the applicant should consider the factors which may affect the duration of the recall action and should inform the MCAZ. The recall should be completedby the date as directed by the MCAZ. When the required information is available, the appropriate strategy should be proposed by the applicant and/or manufacturer to MCAZ. The proposed recall strategy should be agreed by the MCAZ before implementation and the agreement should be reached in 24hrs of submission of notification form. The actual implementation of the recall includes use of thebasic steps which are summarized in Section B and these will be common to all strategies. In the recall strategy, the applicant should mention the following:

i. Indicate the proposed level in the distribution chain to which the recall is extending (see level of recall below), if the recall only extends to the wholesale level, the rationale of not recalling to retail level should be explained;
ii. In case of consumer level recall, additional information should be mentioned-
iii. Indicate the location of recall distribution channels for consumers;
iv. Indicate the proposed refund mechanism at the recall distribution channels, the conditions of refund (applicable to opened products, expired products or parallel-imported products) and methods of refund (by means of money, credit notes or product replacement etc.);
v. Indicate the method of notification;
vi. Indicate how the message of recall will be delivered to customers e.g. press release or recall letters etc;
vii. If the applicant and/or manufacturer has a website, it should consider posting the recall notification on it as an additional method of recall notification;
viii. Report on what have the customers been instructed to do with the recalled product;
ix. It is necessary for recalling firms to know the name and title of the recall contact person for each of its consignees. Addressing a recall letter to a recall contact person will expedite the recall process and reduce the potential for the recall letter to get misdirected;
x. If product is to be returned, explain the mechanics of the process;
xi. Explain if the recall will create a market shortage that will impact on the consumer;
xii. Provide a proposed disposal plan of the recalled products, whether they would be destroyed, reconditioned or returned to the external or local manufacturer; and
xiii. Inform MCAZ before product destruction, the proposed method of destruction would be reviewed and MCAZ may choose to witness the destruction. The destruction Certificate of the product should be submitted to the MCAZ.

5.5 CLASSIFICATION OF RECALLS

Recalls are classified according as follows:

5.5.1 Class I recall

Occur when products are potentially life-threatening or could cause a serious risk to health. Examples of Class I Defects

i. Wrong Product (label and contents are different products)
ii. Correct product but wrong strength, with serous medical consequences
iii. Microbial contamination of sterile injection or ophthalmic product
iv. Chemical contamination with serious medical consequences
v. Mix up of some products with more than one container involved
vi. Wrong active ingredient in a multi-component product with serious medical consequences
vii. Lack of effectiveness for a life threating condition.

5.5.2 Class II recall

Occur when product defects could cause illness or mistreatment, but are not Class I. Examples of Class II Defects

i. Mislabelling e.g. wrong or missing text or figures
ii. Missing or incorrect information- leaflets or inserts
iii. Microbial contamination of non-injectable, non-ophthalmic sterile product with medical consequences
iv. Chemical/ physical contamination (significant impurities, cross-contamination, particulates)
v. Mix up of products in containers
vi. Non-compliance with specification (e.g. assay, stability, fill/ weight or dissolution)
vii. Insecure closure with serious medical consequences (e.g. cytotoxics, child resistant containers, potent products)
viii. Lack of efficacy/effectiveness for medical condition that is not life threatening.

5.5.3 Class III recall

Occur when product defects may not pose a significant hazard to health ie low risk to health but recall may be initiated for other reasons, due to quality, safety or efficacy concerns. Examples of Class III Defects;

i. Faulty packaging e.g. wrong or missing batch number or expiry date.
ii. Faulty closure.
iii. Contamination- microbial spoilage, dirt or detritus, particulate matter.

Class I or Class II recalls are considered to be urgent safety-related recalls. They must be reported to the MCAZ for further evaluation and investigation. Class III recalls are considered to be minimum risk to public health but should however still be reported to the MCAZ.
Note: Each recall is a unique exercise and there may be occasions when the scope of a recall can be narrowed to particular customer groups. The classification is determined by the

MCAZ. Expert advice might be sought where the nature of the hazard or its significant is not clear. Decision made by other stringent regulatory authorities internationally will also be considered.

The Guidelines do not apply to the recall of a medicine, vaccine or medical device related to regulatory issues such as cancellation of registration due to non-payment of retention fees, approved change of applicant, manufacturer, labelling, package insert or other registered particulars. Regulatory issues in which there is lack of compliance to current Good Manufacturing Practices may lead to a recall and/or a cancellation of registration.

5.6 LEVELS OF RECALL

As with classification, the level (or depth) of a recall is to be assigned in agreement with the MCAZ. In determining the recall level, the principal factors to be considered are the significance of the hazard (if any), the channels by which the medicine, vaccine or medical device pharmaceutical products have been distributed, and the level to which distribution has taken place. Again, expert opinion may be necessary to determine the significance of the hazard or risk. There are three levels of recall: wholesale, retail and consumer.

5.6.1 Wholesale level

Includes all parties involved in wholesale distribution and may include wholesalers and retail pharmacies.

5.6.2 Retail level

Includes:

i. All public and private hospital pharmacies;
ii. Retail pharmacies, Industrial, Government and Council owned clinics;
iii. Clinical investigators and the institutions in which clinical investigations are performed;
iv. Medical, dental and other health care practitioners;
v. Nursing homes and other related institutions;
vi. Other retail outlets e.g. medicine shops, supermarkets and health food stores;

***NB**: In the case where consumers that are known to be in possession of the affected products, a plan should be put in place where specific telephone calls are made to these consumers or recall letters sent to arrange for return of the recalled product.*

5.6.3 Consumer level

Includes patients and other consumers.

5.7 COMMUNICATION TO PUBLIC

5.7.1 Recall letters

In case of a recall, the applicant and manufacturer may prepare letters 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. The recall communication shall not contain any material that can be viewed as promotional in nature. The letter may be sent by mail, facsimile or e-mail to the clients. The recall letter needs prior approval by the MCAZ unless the matter is urgent and there is immediate hazard or risk to the patients. The letter may also be referred to as alert notice or dear doctor letter. The MCAZ may also write a circular on the recall in addition to the letter from the applicant, and manufacture.

The recall letter should use company letterhead; include date and name and title of signatory. The text of recall letter may include:

i. Description of the medicinal product: name of the product; Zimbabwe registration number; name of manufacturer, pack size; dosage form; batch number(s) and expiry date;
ii. Hazard and risk associated with the product: The reason for the recall should be concisely explained. It should be made clear that further distribution or use of the product should cease immediately.
iii. Instruction for recall of the product: The method of return, disposal or correction and refund mechanism of the product. Proof of delivery of communication by the healthcare professional e.g., read receipt of an e-mail or list of addresses for recall letters that are posted is acceptable. Each posted recall letter could contain a "Return to Sender" address and the recall agency will be able to evaluate which Healthcare professional have not received the letters. The applicant/or manufacturer should clearly identify a hotline number for enquiry.

For retail level recall, the applicant should have confirmation for returning all the stock on hand from the consignees using the Recall Reply Form (LEF 61). As the Distributor has batch traceability records it is acceptable that the Distributor send out the Recall Reply Form (LEF 61) to their customers and follow-up with non-responders. Responsibilities in the case of a recall must be defined in the Quality Assurance Agreement between applicant and their chosen distributor.

If safety to the public is involved and distribution is limited, the applicant 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 3 months to ensure that product still in transit or on its way to retail or hospital is adequately managed and quarantined.

5.7.2 Press Release approved by MCAZ

Rapid alert to public is usually reserved for hazards classified as Class I, and where appropriate Class II, or situation where other means for controlling the hazard appear inadequate. Rapid alert to public may be issued through appropriate channels which may

include press release approved by the MCAZ. Please note that all press release statements associated with a product Defect and Recall must be approved by MCAZ prior to publication or release in the press to avoid unnecessary panic to the public and consumers or miscommunications. Information that should be included in the media statements is:

i. Clear outline of the problem
ii. Clear product information identifying the product use
iii. Possible effects (without creating fear to the consumer)
iv. What should the consumer do
v. Company information and contact details of responsible person(s)

5.7.3 Recall publication on MCAZ Website

Medicines Recalls and Notifications are published on a dedicated section of our website. The publishing of a Medicine Recall or Notification automatically triggers an email notification to anyone who has registered to receive such notifications. Any individual can sign up via our e-mail alerting service.

5.8 RESPONSIBILITIES OF APPLICANT, PRINCIPALS AND MANUFACTURERS

5.8.1 The applicant and manufacturer has responsibilities in relation to recall of medicines, vaccines and/or medical devices products in three general areas:

i. in maintaining records and establishing procedures which will assist in facilitating recall should such action become necessary; and
ii. in taking the prime responsibility for implementing recall in the situation where it is necessary.
iii. In further investigating the case of the product defect and recall and providing the corrective and prevention actions

5.8.2 Records

The applicant, distributors and manufacturer should maintain records for all the medicines manufactured or distributed by them in accordance with the following:

5.8.3 For manufacturers

i. A system should be in operation whereby the complete and up-to-date histories of all batches of products from the starting materials to the finished products are progressively recorded;
ii. The system should allow the determination of utilization and disposal of all starting materials and bulk products.

5.8.4 For distributors

i. Records of all sales or distribution (including professional samples and export to other countries) of medicines, vaccines and/or medical devices should be retained or kept readily accessible to permit a complete and rapid recall of any lot or batch of a pharmaceutical product.
ii. The complete records pertaining to manufacturing and distribution should be retained for two years after the date of transaction or one year after the expiry date of the batch whichever longer.
iii. Besides, the applicant and manufacturer should retain records of problem reports received about each product. Problem reports should be evaluated by competent personnel and appropriate action taken. The evaluation of each report and the action taken should be shown in the records.
iv. All the above records should be readily available and easy to follow so as to expedite a recall whenever necessary. A copy of manufacturing/ import and distribution records should be sent to the MCAZ when a recall is implemented.

***NB**. In some cases due to the parallel importation of medicines into Zimbabwe, the importer and/or distributor will be responsible to liaise with the external applicant and the manufacturer to comply with MCAZ medicine recall and defect guidelines and decisions.*

5.9 RECALL PROCEDURE

As mentioned in Section 5.2 applicant should prepare procedures for recall action which are consistent with the Guidelines and which are applicable to their own operations. All senior personnel should be familiar with their responsibilities in connection with the procedure and of the records system for pharmaceutical products.

5.9.1 Problem Reporting

Where evaluation of a problem report concerning a medicine indicates that recall may be necessary, the report must be conveyed with the least possible delay to the MCAZ, including medicines that have been exported-only and not supplied in Zimbabwe. Any batch of a formulated product that has been distributed, or any batch of a starting material that is found not to comply with the approved product specifications or a relevant standard of the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PICS), must also be reported if it has been used in a distributed product.

5.9.2 Recall

i. Applicant has the prime responsibility for implementing recall action, and for ensuring compliance with the recall procedure at its various stages (Section B). **However, no recall, regardless of class of recall, should be undertaken without consultation with the MCAZ.**

ii. A responsible personnel for recall should be appointed to coordinate the recall and his/her name and contact phone number should be notified to the MCAZ. In addition, this personnel has to report the progress of recall regularly to the MCAZ.
iii. For Class I recall, applicant and manufacturer should notify its clients within 24 hours upon the decision of recall and quarantine undistributed stock immediately. The company personnel may be utilized to immediately disseminate information on the recall. This includes telephone advice to quarantine stock pending recall or possible recall followed by recall letters if necessary. A Recall Reply Form (LEF 61) should be sent to all consignees to confirm quantity of stock on hand and have all of them returned. The Recall Reply Form (LEF 61) should be kept for inspection by the MCAZ. All Class I recalls should be completed within a time as found suitable for the case agreed by the MCAZ.
iv. For consumer level recall, the applicant and manufacture should set up sufficient recall distribution channels for collection of recalled products. Information of location of the recall distribution channels their operating hours and duration, conditions of refund as well as method of refund should be noticed to consumers by effective means.
v. Applicant and manufactures representatives may be utilized to recover stock which is the subject of recall, providing the provisions are observed in relation to unauthorized possession of certain stock, e.g. narcotics
vi. Applicant may also be required to notify external recipients of recall actions that affect them.

5.9.3 Refund Mechanism

Applicant, manufacture and distributor should set up a refund mechanism for the recalled products and is responsible for the refund.

5.9.4 Post-recall

After the timeframe directed by the MCAZ to complete the recall, or at other agreed times, the applicant is to provide the MCAZ with an interim report during the recall process for the monitoring of progress within 7 calendar days after initiation of the recall. The interim report should contain the following information:

i. the number of organizations or persons to whom the defective product has been supplied;
ii. the date and means of notifying them of the recall;
iii. the number of responses received from them;
iv. the names of the non-responders;
v. the quantity of stock returned;
vi. the quantity of stock that has been off shelves pending return to applicant;
vii. the estimated time frame for the completion of the recall.

A Final Report Form (LEF 60) containing the following information should be submitted to MCAZ within 14 calendar days after commencing of the recall:

i. the circumstances leading to the recall;
ii. the consequent action taken by the applicant or manufacturer;
iii. the extent of distribution of the relevant batches in Zimbabwe and external; -

iv. the result of the recall
v. the quantity of stock returned, corrected, outstanding;
vi. the quantity of stock used by the consignees and;
vii. the quantity of stock not located;
viii. date of recall completion;
ix. confirmation using Recall Reply Form (LEF 61) where practicable, the retailers have returned all the recalled products to the applicant or manufacture and the customers have received the recall letter;
x. the method of destruction or disposal of the recalled products; and

The applicant or manufacture should report to MCAZ 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 MCAZ in a timely manner, not more than 30 calendar days after the recall.

NB. *These reports establish the effectiveness of the recall and unless satisfactory reports are received, further recall action may have to be considered.*

5.10 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.

5.10.1 Check on the Effectiveness of Recall Action

It is the applicant and manufacturer responsibility to assure that the recall is effective. The MCAZ examines the recall reports and the signed Recall Reply Form (LEF 61) submitted by the applicant and assesses the effectiveness of the recall action. Recall records may be inspected and in some case the MCAZ may contact a percentage of customers in the distribution list as a means of assuring that the applicant is carrying out its recall responsibilities. If MCAZ finds the recall to be ineffective, the applicant and/or manufacture will be asked to take appropriate steps, including re-issuing recall letters.

5.10.2 Investigation of the Reasons for Recall and Initiation of Remedial Action

On completion of a recall, the applicant and manufacture are requested to 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 are not apparent, investigation and in some cases current Good Manufacturing Practice (cGMP) audits may be necessary, including a product- based cGMP inspection conducted by MCAZ inspectors.

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.

5.11 REINSTATEMENT OF SUPPLY

5.11.1 The quality of the products shall conform to specific requirements including finished product specifications before resuming the supply to public. **The applicant and manufacture must seek approval from the MCAZ for reinstatement of the medicine and/or vaccine/medicaldevice previously "totally recalled".**

5.11.2 Implementation of Remedial Action

The applicant 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 and/or reduce impurities and degradation products etc.

5.11.3 Submission of Analytical Report

After implementing the remedial action and subsequent manufacturing or importing the new batch of the product, the applicant shall submit analytical report(s) of the new batch tested by external accredited laboratory to the MCAZ 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 MCAZ for verification. If MCAZ 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 MCAZ. After evaluation, the MCAZ would inform the applicant whether the submitted reports are satisfactory.

5.11.4 Verification of corrective action

When the MCAZ is satisfied by the submitted reports, samples of the first batch of the product (being manufactured by the local manufacturer / being imported) will be collected for examination by the MCAZ before the product can be distributed. After the MCAZ 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 will be borne by the applicant and/or manufacturer. Where necessary a third party independent analysis maybe required in exceptional cases at the cost of the manufacturer or applicant after approval by the MCAZ.

5.12 METHODOLOGIES FOR DETECTING AND PREVENTING SUBSTANDARD AND FALSIFIED MEDICINES AND MEDICAL DEVICES

5.12.1 Maintaining a public database of authorized products, marketing authorization holders and authorized pharmaceutical manufacturers

The MCAZ keeps a record of marketing authorization decisions and the registers that detail the authorized products and pharmaceutical manufacturers. This assists not only the procurement and distribution networks, but also to other regulatory authorities. In the context of detecting and responding to SF medical products, these databases are useful in the correct characterization of a suspected product.

5.12.2 Code of conduct/ethics for regulators

The MCAZ regulatory officers have a professional and ethical responsibility to maintain the highest standards of professional conduct in exercising their professional duties, as they play a pivotal role in ensuring compliance with applicable laws and regulations in the development and commercialization of health care products. Observance of codes of conduct and ethical principles might help to prevent SF medical products from entering the legal supply chain.

5.12.3 Inspections at ports of entries

Inspections at borders include administrative and other safeguards aimed at ensuring that consignments of imported medicinal products are in full conformity with the relevant import permits and that they remain secure within the distribution chain. (refer to import and export guidelines)

5.12.4 Authentication and detection technologies

Authentication technologies comprise several solutions applied to the original medical product, especially to the packaging, to enable the verification of genuineness of medicine samples by MCAZ, industry representatives, government officers or even the public. These technologies also act as a deterrent to anyone considering production and distribution of SF medical products as they make the production and distribution of a convincingly falsified medical product more difficult and costly. In contrast, detection technologies are those used in the identification of SF medical products, ranging from a visual analysis of authentication technologies to a full chemical analysis in a laboratory setting.

5.12.5 Risk-based post-marketing surveillance

According to WHO, regular sampling and surveying of both the regulated and unregulated supply chains is a way of identifying SF medical products. Different methodologies are used to sample the market and range from random sampling to targeted sampling of particular

products and outlets. It is important to optimize the use of resources by focusing surveillance activities on those products and venues that pose a higher risk to patients. Risk-based post-marketing surveillance might be a very effective tool in the detection of SF medical products.

Note:

1. **Attachment I:** Medicine, Vaccine or Medical Device Product Problem/defect Report Form (LEF 63) should be used to report problem of Medicine, Vaccine or Medical Device products on quality, safety or efficacy, which are thought to have arisen during manufacture, storage, or handling. Problems of this nature are usually found in a singlebatch of a product and may require laboratory analysis investigation by the MCAZ.
2. **Attachment II:** Recall notification Form (LEF 62) should be filled when decisionof a recall is established.
3. When the reported problem may lead to Class I or II recall, it should be reported to theMCAZ ***within 48 hours*** by written letter or email of this scanned form (Attachment 1) Medicine, Vaccine or Medical Device Product Problem/Defect Report Form (LEF 63)
4. If Class I or II recall is required, LEF 63 and LEF 62 forms should be reported to the MCAZ immediately by email or signed letter.
5. The applicant shall NOT wait to submit this information until ALL applicable information in **LEF 62** is prepared and assembled prior to notification to the MCAZ.
6. For problem or defect that may lead to Class III recall, Medicine, Vaccine or MedicalDevice Product Problem/Defect Report Form (LEF 63) should be returned by email and signed letter to MCAZ ***not later than 72 hours***. When Class III recall is required, the scanned forms LEF 63 and LEF 62 should be submitted by email and signed letter.
7. **Attachment III** Recall Reply Form (LEF 61)
8. **Attachment IV** Final Report Form (LEF 60)
9. **Attachment V** Report on medicinal (Pharmaceutical) Product defect or problem for completion by all other parties (healthcare professionals and the public) except the manufacturer.
10. **Attachment VI** Product Defects Risk Assessment Form (LEF 86)

Please submit all completed forms and signed letters and emails to the Director-General, Medicines Control Authority of Zimbabwe (MCAZ), 106 Baines Avenue, Harare, Telephone: 708255/792165; Cell 0772145191-3 Email: mcaz@mcaz.co.zw, Website: www.mcaz.co.zw

CONTACT DETAILS

Address:	Medicines Control Authority of Zimbabwe
	106 Baines Avenue
	P.O Box 10559
	Harare
	Zimbabwe
Telephone number:	0242 736981-5; 708255; 2901327-31
Whatsapp number:	0718 855 934
Email addresses:	mcaz@mcaz.co.zw

6.0 KEY RELEVANT DOCUMENTS

6.1 Medicines and Allied Substances Control Act *(Chapter 15:03)*

6.2 Medicines and Allied Substances Control (General) Regulations, 1991, SI 150 of 1991

6.3 Zimbabwe National Pharmacovigilance Policy and Guidelines Handbook

6.4 Guidelines on the Import and Export of Registered Medicines

6.5 Guideline for Licensing and Enforcement Division, Code of Conduct for Inspectors

6.6 Guideline on Post Marketing Surveillance

7.0 HISTORY

DOCUMENT HISTORY		
Revision Number	Date Approved	**5.7.3** Changed from **Recall publication on MCAZ Website** Medicines Recalls and Notifications are published on a dedicated section of our website. Changed to **Recall publication on MCAZ Website** Medicines Recalls and Notifications are published on a dedicated section of our website. The publishing of a Medicine Recall or Notification automatically triggers an email notification to anyone who has registered to receive such notifications. Any individual can sign up via our e-mail alerting service. **5.12** **Added** **METHODOLOGIES FOR DETECT AND PREVENT SUBSTANDARD AND FALSIFIED MEDICINES AND MEDICAL** **Added** **5.12.1 Maintaining a public database of authorized products, marketing authorization holders and authorized companies**
0	February 2022	

		The MCAZ keeps a record of marketing authorization decisions and the registers that detail the authorized products and companies. This assists not only the procurement and distribution networks, but also to other regulatory authorities. In the context of detecting and responding to SF medical products, these databases are useful in the correct characterization of a suspected product or transaction. **5.12.2 Code of conduct/ethics for regulators** The MCAZ regulatory officers have a professional and ethical responsibility to maintain the highest standards of professional conduct in exercising their professional duties, as they play a pivotal role in ensuring compliance with applicable laws and regulations in the development and commercialization of health care products. Observance of codes of conduct and ethical principles might help to prevent SF medical products from entering the legal supply chain. **5.12.3 Inspections at borders** Inspections at borders include administrative and other safeguards aimed at ensuring that consignments of imported medicinal products are in full conformity with the relevant import permits and that they remain secure within the distribution chain. (refer to import and export guidelines) **5.12.4 Authentication and detection technologies** Authentication technologies comprise several solutions applied to the original medical product, especially to the packaging, to enable the verification of genuineness of medicine samples by MCAZ, industry representatives, government officers or even the public. These technologies also act as a deterrent to anyone considering production and distribution of SF medical products as they make the production and distribution of a convincingly falsified medical product more difficult and costly. In contrast, detection technologies are those used in the identification of

		SF medical products, ranging from a visual analysis of authentication technologies to a full chemical analysis in a laboratory setting. **5.12.5 Risk-based post-marketing surveillance** According to WHO, regular sampling and surveying of both the regulated and unregulated supply chains is a way of identifying SF medical products. Different methodologies are used to sample the market and range from random sampling to targeted sampling of particular products and outlets. It is important to optimize the use of resources by focusing surveillance activities on those products and venues that pose a higher risk to patients. Risk-based post-marketing surveillance might be a very effective tool in the detection of SF medical products.