PHARMACY, MEDICINES & POISONS BOARD

GUIDELINES FOR RECALL OF MEDICINES AND HEALTH PRODUCTS IN MALAWI

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1. INTRODUCTION

The Malawi Pharmacy Medicines and Poisons Board (PMPB) was established under the PMP Act No. 15(1988) to provide for comprehensive assurance that medicines and other medicines and health products including medical devices and vaccines in use in both the public and private healthcare systemin Malawi are safe, efficacious and of the acceptable quality.

In spite of various regulatory measures being implemented by the board including registration, inspection, control of distribution, quality control and pharmacovigilance, among others, the challenge of recall of expired, counterfeit, substandard, unwanted and useless donations continue to recur. Hitherto, recalls have been in an uncontrolled and uncoordinated manner and have been done without recourse to the PMPB. The Board is therefore unable keep a database of recalls to ensure that they do not return to the supply chain.

These guidelines have therefore been developed to provide guidance to medicines and health products importers, manufacturers and manufacturer's representatives and the medicines donors on how undertake, report and manage a recall when the need arises.

It also defines the actions to be taken by PMPB and the product license holder to ensure that, medicines and other healthcare products with suspected or proven safety, quality and efficacy issues are removed from the market.

PMPB is responsible for recall/withdrawal of medicines and will closely monitor the effectiveness of the holder of registration certificate/parallel importers recall actions and provide scientific, technical and operational advice.

These guidelines serve to remind the holder of certificate of registration/Parallel importer that PMPB expects them to take full responsibility of medicine recalls including follow-up checks to ensure that the recalls are successful.

Most recalls are conducted on voluntary basis. PMPB may recall medicines when they are substandard or counterfeit. If the recalling performance is deemed in adequate,PMPB is prepared to take appropriate actions to remove the product from sale or use.

2. DEFINITIONS

2.1 Product License Holder

Is the person or business which could be the manufacturer, importer, distributor or the registration certificate holder of a medicinal/pharmaceutical product and has the primary responsibility for the supply and distribution of the product in Malawi.

2.2 Medicine

Under the Pharmacy and Poisons Act, Medicine: means any substance or mixture of substances used or purporting to be used for manufacture of sold for use in-

1. Diagnosis, treatment, mitigating,correcting or modifying or prevention of a disease, abnormal, physical, or mental state in the symptoms there of in man.
   or

2. Restoring, correcting or modifying any somatic or psychic or organic function in man and includes any veterinary medicine.

2.3 Recall

Recall is a process for withdrawing or removing a pharmaceutical 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 counterfeit. The recall might be initiated by the manufacturer, wholesale dealer, product license holder, or the Pharmacy, Medicines and Poisons Board.

3. RECALL CLASSIFICATION

Recalls are classified based on either the level of risk posed by the reason for the recall and/ or the extent and depth of recall.

3.1 Risks

3.1.1 Class I recalls.

They occur when products are potentially life-threatening or could cause a serious risk to health.

Examples of Class I Defects

1. Wrong Product (label and contents are different products)
2. Correct product but wrong strength, with serous medical consequences
3. Microbial contamination of sterile injection or ophthalmic product
4. Chemical contamination with serious medical consequences
5. Mix up of some products (‘rogues’) with more than one container involved
6. Wrong active ingredient in a multi-component product with serious medical consequences

3.1.2 Class II recalls

They occur when product defects could cause illness or mistreatment, but are not Class I.

Examples of Class II Defects

1. Mislabeling e.g. wrong or missing text or figures
2. Missing or incorrect information- leaflets or inserts

3. Microbial contamination of non-injectable, non-ophthalmic sterile product with medical consequences
4. Chemical/ physical contamination (significant impurities, cross contamination, particulates)
5. Mix up of products in containers (“rogues”)
6. Non-compliance with specification (e.g. assay, stability, fill/ weight or dissolution)
7. Insecure closure with serious medical consequences (e.g. cytotoxics, child resistant containers, potent products)

3.1.3 Class III recalls

They occur when product defects may not pose a significant hazard to health, but withdrawal may be initiated for other reasons.

Examples of Class III Defects

1. Faulty packaging e.g. wrong or missing batch number or expiry date
2. Faulty closure
3. 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 Pharmacy, medicines and Poisons Board for further evaluation and investigation.
Class III recalls are considered to be non safety-related recalls.
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 Pharmacy, medicines and Poisons Board. Expert advice might be sought where the nature of the hazard or its significant is not clear.

3.2 Level

The level (or depth) of a recall is to be assigned by Pharmacy, medicines and Poisons Board. In determining the recall level, the principal factors to be considered are the significance of the hazard (if any), the channels by which the medicines and health products have been distributed, and the level to which distribution has taken place.
There are three levels of recall: wholesale, retail and consumer.

3.2.1 Level / Type A

Wholesale level which includes:

1. All parties involved in wholesale distribution and may include wholesalers and retail pharmacies.

3.2.2 Level/ Type B

Retail level which includes:

1. All public and private hospital pharmacies.
2. Retail pharmacies.
3. Clinical investigators and the institutions in which clinical investigations are performed.
4. Medical, dental and other health care practitioners.
5. Nursing homes and other related institutions.
6. Other retail outlets e.g. medicine shops, supermarkets and health food stores.
7. Wholesale level.

3.2.3 Level/ Type C

Consumer level which includes:

1. Patients and other consumers; and
2. Wholesale and retail levels.

4. STEPS IN THE RECALL PROCEDURE

The steps to be followed in the recall of unwanted medicines and health products in Malawi shall be divided into six stages as set out below.

4.1 Notification of a Pharmaceutical Product Problem

Recall might be initiated as a result of reports or complaints referred to the product license holder by manufacturers, wholesalers, retailers and hospital pharmacies, research institutes, medical practitioners, dentists and patients on the quality, safety or efficacy of a medicine or health product.

Recall might also be initiated as a result of test carried out by the quality control laboratory of the PMPB on samples of a product obtained from post marketing sampling or based on request of international companies or health authorities.
To ascertain the validity of reports of defects calling for recall, certain information is required to be provided to determine the appropriate method to be used. The Medicines and health products problem report form of the Pharmacy, medicines and Poisons Board (Appendix ONE) shall be used.

Class I or Class II recalls must be reported to the Pharmacy, medicines and Poisons Board within 24 hours after receipt of the complaint or report for investigation. The MHPP may be submitted together with opinions on toxicological or therapeutic hazards and the action proposed by the authorities/ organization (if any).
For less serious problems that would result in a Class III recall, the MHPP form should be sent to Pharmacy, medicines and Poisons Board no later than 72 hours after receipt of complaint or report of a problem.

All forms should be submitted to the Pharmacy, medicines and Poisons Board prior to the decision on recall by the product license holder.
When the need for recall has been established, additional information is required so that an appropriate recall strategy may be devised. A summary of the information required is provided in Section B.

4.2. Initiation of Recall/ Information Required For Assessment of Recall

When a decision is made to initiate a recall on a medicine or health product, the product license holder is required to notify the PMPB of the recall situation with the Medicine and Health Product Recall Notification Form (MHPRNF) (Appendix TWO). This form could be submitted prior to official notification to enable the Pharmacy, medicines and Poisons Board

to review and comment on the written notification and to offer guidance and assistance in the recall process.

The information required may include:

1. Details of the Problem.
2. Name, telephone and facsimile number of the person reporting the problem.
3. Date of report.
4. Physical location of the problem.
5. Nature of the problem.
6. Number of similar report received.
7. Results of tests and other investigations on suspect or other samples.
8. Details of the Product.
9. Name of the product and description including active ingredients, dosage from, strength, registration no, pack size or type.
10. Batch number(s) and expiry date.
11. Manufacturer/ distributors and contact telephone, facsimile numbers and email address.
12. Date manufactured, date released or imported into Malawi.
13. Quantity of the batch, date and amount manufactured, released or imported into Malawi
14. Local distribution list.
15. Oversea distribution list of product exported from Malawi.
16. Whether the product is meant to be sterile.
17. Health hazard evaluation and proposed action.
18. Type of hazard, and evaluation of health hazard to user.
19. Action proposed by the Product license holder.
20. Proposed recall classification and level.
21. Availability of alternative product.

4.3. Assessment of Recall

4.3.1 Recall Strategy

Each recall shall be treated on its own merit. A number of factors are common to all recalls that need to be considered in deciding on the 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 Product license holder should consider the factors which may affect the duration of the recall action and should inform the Pharmacy, medicines and Poisons Board. The recall should be completed by the date as directed by the Pharmacy, medicines and Poisons Board.

When the required information is available, the appropriate strategy should be proposed by the Product license holder to Pharmacy, medicines and Poisons Board and this shall be agreed by the Pharmacy, medicines and Poisons Board before implementation.

In the recall strategy, the Product license holder should mention the following:

1. Indicate the proposed level in the distribution chain to which the recall is extending

2. If the recall only extends to the wholesale level, the rationale of not recalling to retail level should be explained;
3. In case of *consumer level* recall, additional information should be mentioned-
4. Indicate the location of recall spots for consumers (preferably not less then 10 recall spots covering different district in Malawi), their operation time and duration (at least 7 days);
5. Indicate the hotlines number(s) for enquiry and the corresponding operating hours;
6. Indicate the proposed refund mechanism at the recall spots, 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.);
7. Indicate the method of notification (e.g. mail, phone, facsimile, email);
8. Indicate how the message of recall will be delivered to customers e.g. press release or recall letters etc;
9. If the Product license holder has a website, it should consider posting the recall notification on it as an additional method of recall notification;
10. Report on what the customers been instructed to do with the recalled product;
11. -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;
12. If product is to be returned, explain the mechanics of the process;
13. Explain if the recall will create a market shortage that will impact on the consumer;
14. Determine and provide the course of action for out-of-business distributors;
15. Provide a proposed disposal plan of the recalled products, whether they would be destroyed, reconditioned or returned to overseas manufacturer; and
16. Inform Pharmacy, medicines and Poisons Board before product destruction. Such destruction shall be in accordance with guidelines approved by the Board.

4.4 Communication to Public

4.4.1 Recall letters

In case of a recall, the Product license holder 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 letter may be sent by mail, facsimile or e-mail to the clients.

The recall letter should use company letterhead; include date and name and title of authorized person or responsible Pharmacist.

The text of recall letter may include:

1. **Description of the pharmaceutical product:** name of the product; Malawi registration number; name of manufacturer, pack size; dosage form; batch number(s) and expiry date;
2. **Hazard 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.

3. **Instruction for recall of the product:** The method of return, disposal or collection and refund mechanism of the product. There should be a request for a response to confirm receipt and understanding of the action to be taken e.g. pre-addressed cards, telephone replies or a form to complete and return by facsimile or e-mail. The Product license holder should clearly identify a hotline for enquiry.
    i. For retail level recall, the Product license holder should have confirmation for returning all the stock on hand from the consignees using the Recall Reply Form at Appendix 3.
    ii. If safety to the public is involved and distribution is limited, the Product license holder may contact the clients of the information listed above by telephone and followed by a recall letter.

4.4.2 Press Release

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.

The media release should contain sufficient information to describe the product and a clear outline of the problem(without causing unnecessary alarm) and must state appropriate response by consumer or client.

4.5 Responsibilities of Product License Holders

Product license holder has responsibilities in relation to recall of medicines and health products in two general areas:

1. Maintaining records and establishing procedures which will assist in facilitating recall should such action become necessary; and
2. Taking the prime responsibility for implementing recall in the situation where it is necessary.

4.5.1 Records

The Product license holder should maintain records for all the medicines and health products manufactured or distributed by them in accordance with the followings:

4.5.1.1 For manufacturers

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.

The system should allow the determination of utilization and disposal of all starting materials and bulk products.

4.5.1.2 For distributors

Records of all sales or distribution (including professional samples and export to other countries) of medicines and health products should be retained or kept readily accessible to permit a complete and rapid recall of any lot or batch of a medicines and health product.
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 is longer.

Besides, the Product license holder 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.

All the above records should be readily available and easy to follow so as to expedite recall whenever necessary. A copy of manufacturing/ import and distribution records should be sent to Pharmacy, Medicines and Poisons Board when a recall is implemented.

4.5.2 Recall Procedure

Product license holders 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 procedures and of the records system for medicines and health products.

4.5.3 Problem Reporting

Where evaluation of a problem report concerning medicines and health products indicates that recall may be necessary, the report must be conveyed with the least possible delay to the Pharmacy, medicines and Poisons Board.
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 SADC, must also be reported if it has been used in the distributed products.

4.5.4 Recall

Product license holder 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 level, should be undertaken without consultation with the Pharmacy, medicines and Poisons Board.

A responsible officer for recall should be appointed to coordinate the recall and his/her name and contact phone number should be notified to Pharmacy, medicines and Poisons Board. In addition, this officer has to report the progress of recall regularly to the Pharmacy, medicines and Poisons Board.

For Class I recall, Product license holder should notify its clients within 24 hours upon the decision of recall.

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 (Appendix 3) should be sent to all consignees to confirm quantity of stock on hand and have all of them returned. The reply form should be kept for inspection by Pharmacy, medicines and Poisons Board.

All Class I recall should complete within a time as found suitable for the case agreed by Pharmacy, medicines and Poisons Board.

For consumer level recall, the Product license holder should set up sufficient recall spots for collection of recalled products. Information of location of the recall spots, their operating hours and duration, conditions of refund as well as method of refund should be noticed to consumers by effective means.

Company representatives may be utilized to recover stock which is the subject of recall, provided the provisions are observed in relation to unauthorized possession of certain stock, e.g. dangerous drugs.

Product license holder may also be required to notify overseas recipients of recall actions that affect them.

4.5.5 Refund Mechanism

Product license holder should set up a refund mechanism for the recalled products.

4.5.6 Post-recall

The product license holder is to provide the Pharmacy, Medicines and Poisons Board with an interim report during recall process within 7 days after initiation of recall

The interim report should contain the following information:

1. The number of organizations or persons to whom the defective product has been supplied;
2. The date and means of notifying them of the recall;
3. The number of responses received from them;
4. The names of the non-responders;
5. The quantity of stock returned;
6. The quantity of stock that has been off shelves pending return to Product license holder;
7. The estimated time frame for the completion of the recall .

A final report contain the following information should be submitted to Pharmacy, medicines and Poisons Board within 14 days after commencing of the recall:

1. The circumstances leading to the recall;
   i. The consequent action taken by the Product license holder;
   ii. The extent of distribution of the relevant batch in Malawi and overseas;

2. The result of the recall
   i. The quantity of stock returned, corrected, outstanding;
   ii. The quantity of stock used by the consignees and;
   iii. The quantity of stock not located;
   iv. Date of recall completion;

3. Confirmation (using Recall Reply Form at Appendix 3), where practicable, the retailers have returned all the recalled products to the Product license holder and the customers have received the recall letter.

4. The method of destruction or disposal of the recalled products.

The Product license holder should report to Pharmacy, medicines and Poisons Board with relevant explanation and obtain its approval if the final report cannot be submitted within 14 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 Pharmacy, medicines and Poisons Board in a timely manner.

4.6 Evaluation of the Recall

Two issues constitute the evaluation of the recall

i. A check on the effectiveness of the recall
ii. An investigation of the reason for the recall and remedial action taken to prevent a recurrence of the problem.

4.6.1 Check on the Effectiveness of Recall Action

It is the product license holder's responsibility to assure that the recall is effective.
The Pharmacy, medicines and Poisons Board shall examine the recall reports and the signed Recall Reply Forms submitted by the Product license holder and assesses the effectiveness of the recall action. Recall records may be inspected and in some case the Pharmacy, medicines and Poisons Board may contact a percentage of customers in the distribution list as a means of assuring the Product license holder is carrying out its recall responsibilities. If Pharmacy, medicines and Poisons Board finds the recall to be ineffective, the Product license holder will be asked to take appropriate steps, including re-issuing recall letters.

4.6.2 Investigation of the Reasons for Recall and Initiation of Remedial Action On completion of a recall, the Product license holder is requested to provide a report with investigation on the problem and details of the remedial action proposed to prevent a recurrence of the problem which gave rise to the recall. (Section G).

Where a recall is initiated following a report submitted by a party from overseas health authorities, the reporter shall be provided with an outline of the results of investigation and a summary of the recall.

4.7 Reinstatement of Supply

Where the PMPB is satisfied that the product in question has been totally recall and remedial action taken to forestall future occurrence the product license holder may be permitted to reintroduce the product on the market. The quality of the products shall conform to specific requirements before resuming the supply to the public.

4.7.1 Implementation of Remedial Action

The Product license holder shall identify the root cause of the problem and implement the medial action taken corrective action and preventive action (CAPA)

4.7.2 Submission of Analytical Report

After implementing the remedial action and subsequent manufacturing or importing the new batch of the product, the Product license holder shall submit analytical report(s) of the new batch tested by external accredited laboratory to Pharmacy, medicines and Poisons Board as a proof of product quality. The submitted report(s) will be evaluated by the QC Department of the PMPB

After evaluation, Pharmacy, medicines and Poisons Board would inform the Product license holder whether the submitted reports are satisfactory.

4.7.3 Sampling

In addition to the documents submitted above, samples of the product imported after the recall will be sampled for analysis at the QC laboratory of the PMPM. The product can be put on the market only upon approval for reinstatement from Pharmacy, medicines and Poisons Board is obtained.

All costs related to recall process including QC Laboratory analysis shall be incurred by the responsible license holder.