



**GUIDELINES ON
RECALL & RAPID ALERT SYSTEM
For Medicinal Products
(Including Biological & Vaccines)**



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1. Introduction

A recall is an action taken to withdraw/remove a drug from distribution or use including corrective actions for which deficiencies in quality, efficacy or safety have been reported. Quality-related defective products include substandard, adulterated or counterfeit medicinal product. Recalls regarding safety and efficacy include serious adverse reactions and death. The recalls also include medicinal products prohibited under the Pharmacy Profession Law, as well as products whose licenses have been suspended / revoked. The recall applies to all pharmaceuticals, including medicines, biological preparations, cosmetics and medical supplies.

The rapid alert system is the actions taken in the event of warnings, the urgency and seriousness of which does not allow any delay in the alert. An assessment should be made of the severity of the defect and its potential to cause harm to the patient.

2. Background

In the ministerial decree 540/2007, there are references for product recalls stating the right of the EDA to recall a product or any of its batches whether it is pharmaceutical, biological, vaccines or serum according to a specific condition of non-conformity or recall notification of any international organization or adverse reactions other than the known one. so effective and uniform recall procedure, with timelines at every level of supply chain is required.

3. Scope

This guideline applies to all reports of defective product quality and all safety and efficacy incidents reported and received for all medications including vaccines and biologics. This guideline is followed by licensees (manufacturers, importers, agents, distributors, retailers) and recall can be voluntary or statutory. This guideline can be applied by other agencies in the event that urgent action is needed to protect public health or animal health. This guideline will assist in the adoption of the stepwise actions to be followed in the recall strategy also help in assessing recall at each level and compliance with the time frame.

This guideline is mainly applied on the distributed and marketed batches and in case of the non-conformity of batches that has not been marketed no need for the issuing of recall.

4. Definitions

- 🕒 **Recall:** Removal of marketed products for reasons of lack of quality, safety, or efficacy, including labeling that is against the law.
- 🕒 **Batch (es) recall:** The process of removing the selected lot(s) from a product that is found to be defective and poses health risks to consumers if left in the market.
- 🕒 **Batch:** A specific amount of material produced in a process or series of processes that is expected to be homogeneous within certain limits.
- 🕒 **Customer:** Any person, institution or entity that purchases / receives goods from the company for storage, distribution and sale.
- 🕒 **Voluntary Recall:** Recall initiated by a Licensee as a result of an abnormal observation in the quality of any product during a periodic (internal/external) review or investigation of a market complaint or any other failure.
- 🕒 **Statutory Recall:** A recall directed by drug control authorities after verification that a product is in violation of the laws

5. RECALL ACTION CLASSIFICATION

Recall classification assigned to a particular product recall that indicates the relative degree of health hazard by country regulatory authorities.

Class I: A dangerous or defective product that can cause serious health problems or lead to death.

For instance:

- ⦿ Wrong product (label and contents are different products)
- ⦿ Correct product but wrong strength, with serious medical consequences
- ⦿ Microbial contamination of sterile injectable or ophthalmic product
- ⦿ Chemical contamination with serious medical consequences

Class II: A product that may cause a temporary health problem or pose a minor threat of a serious nature.

For instance:

- ⦿ Mislabeling, e.g., wrong or missing text or figures
- ⦿ Missing or incorrect information (leaflets or inserts)
- ⦿ Microbial contamination of non-injectable, non-ophthalmic sterile product with medical consequences

Class III: A product that is not likely to cause a health problem but violates labeling or manufacturing laws and guidelines.

6. LEVELS OF RECALL ACTION

The level (or depth) of product/lotion recall should be determined based on the redemption classification and the level to which it was distributed.

There are three levels of recovery:

Consumer or user level:

Individual consumers, patients, doctors and hospitals.

Retail level:

Call to the level immediately preceding the consumer or user level. It includes pharmacies and hospital pharmacies

Wholesale level:

All levels of distribution between manufacturer and retailer.

All invocations must be executed from

Class I to wholesale/distributor, retail and consumer levels. In such cases, public advertising should be done using print media, electronic, newspapers, television, and radio etc., In addition to obligating the distribution companies to print the recalled item on their sales invoices.

Class II to wholesale and retail levels.

Class III to wholesale levels.

7. Phases of Recall

The Recall Action Process involves the following phases of activity

- An initiation phase when problem identification, risk assessment, the decision on whether to recall, contact with the funding body when appropriate, and the planning for the recall action occurs.
- An implementation phase when the recall action notice is issued by the sponsor and the requested recall action is undertaken.
- A review phase when monitoring and review of the effectiveness of the recall action is undertaken by the sponsor with oversight by authority.

8. Initiation of recall

Any batch of the product that does not meet the specified quality standards must be withdrawn from the market. The recall can be of two types: Voluntary recall and statutory recall.

8.1 Voluntary recall

Manufacturer or importer may voluntarily initiate a recall at any time. Initiation of a recall means a recalling firm's first communication about a voluntary recall, to its direct accounts or to the public. Authority may conduct informal discussions with a manufacturer or distributor that include voluntary recall as an option.

The manufacturer or importer of a medicinal product shall provide the Authority with the following:-

- (a) proprietary name and generic name, dosage form, strength, batch or lot number, pack size, the name and address of the manufacturer, manufacturing date and expiry date;
- (b) The reason for the recall, the nature of the defectiveness or possible defectiveness, the date on and circumstances under which the defects or possible defects were discovered;
- (c) The date on which distribution of the product began;
- (d) area of distribution of the product.
- (e) List of customers to whom product was distributed; and

The manufacturer or importer of a medicinal product should provide the authority with the plan of recall and the timeframe for the recall that is proportional to the class of recall

The manufacturer or importer of a medicinal product shall submit to the Authority a weekly progress report of recall and the final report after completion of a recall which includes reconciliation between delivered and recovered quantities of the product

The manufacturer or importer of a medicinal product shall submit to the Authority an investigation report detailing causes of the defect and corrective and preventive actions undertaken.

In case of the manufacturer or importer non-compliance with the plan of recall the authority will mandate statutory recall.

8.2 Statutory recall:

A statutory recall may be initiated in response to a direction or authorization by the drug authority in one or more of the cases as follows:

1. If it is found that the batch or batches do not comply with the regulatory specifications during the post-marketing surveillance study
2. If it is found that the batch is defective during the investigation of the market complaint.
3. During any random conformity and validity investigation if there is a negative quality impact on the lot already analyzed (e.g., potential for contamination, mixing, deterioration, etc.).
4. If there is any unusual observation during the visual inspection of the retention samples which indicates an effect on the quality of the product after investigation.
5. If the post-marketing monitoring reports or the pharmacovigilance reports indicate the presence of serious safety risks associated with the product.
6. To recall the drug product / batch that is in violation of laws such as non-standard quality
7. Withdrawal of prohibited drugs.
8. in case that there are promotional materials that are in violation of the law or there is an error in the internal bulletins
- 9-Issuance of instructions from international bodies

when evaluation of a reported issue concerning a medicinal product indicates that a recall action may be necessary the classification and level of recall action is determined following discussion between the different departments within the EDA and will involve an assessment of the health hazard presented by the product. The level of recall action will generally reflect the safety risk and distribution pattern of the product.

8.2.1 Factors affecting the statutory recall

A. Risk assessment

The risk assessment includes consideration of the following factors:

- ④ The nature, extent and urgency of possible public health risk
- ④ The likelihood of the issue occurring
- ④ The ability of the consumer, healthcare professional or caregiver to discover/identify the issue should it occurs.
- ④ Whether the product complies with the approved specifications.
- ④ The availability of an alternative product, or the risk associated with not providing treatment if an alternative product is not available.
- ④ Risk of not receiving the correct medication.
- ④ Long-term risk as well as immediate risk.
- ④ In the case of suspicion of defective vaccines (cross contamination with a virus), risk of distorting the analysis in national programs against certain viral diseases.

Further professional assessment of the risk from the product should involve discussion with the manufacturer or importer and include consideration of:

Any other reports which may be related;

- ④ The distribution of the batch (e.g., restricted to known hospitals, widespread through wholesalers).
- ④ Date of first distribution and last distribution.

- ⦿ any remaining stock with the manufacturer or importer.
- ⦿ Probability that other batches are affected in the same way, and their distribution.
- ⦿ If a recall is being considered extremely important issues to consider include:
 - ⦿ possibility of an out-of-stock situation.
 - ⦿ availability of alternative products.
 - ⦿ Clinical effect of a disruption in supply.

B. On-site inspection

On routine investigation or upon complaint unusual observation has been detected and thus a recall action is taken in consideration, some points should be stated in the onsite inspection to help in taking the decision of recall action.

The storage condition should be mentioned to exclude incorrect storage as the cause of the suspected defect.

Visual inspection is a must and identify if the defect is visible and a full description of the defect should be described.

it should be stated was the defect identified in a new previously unopened container or had the container previously been used to exclude user errors such as product mix-ups and so other unopened containers of the same batch available could be checked.

If the product is used with a medical device because in some cases the device could be the cause of the incident

Authority should contact the manufacturer or importer for providing an original pack for the suspected product to make a comparison between the original and suspected pack

C. Previous history.

Previous report of the manufacturing or importing site should be made included and any comment on general GMP compliance and what related products manufactured or imported.

On-site inspection may be required to assess batch records of the product concerned, plant records and records of other batches or products which could also be affected.

Samples may be taken of the batch concerned, related batches and related starting materials. When considering taking material from the company's retained samples, consideration must be given to the quantity available and all tests which may be required for further investigations.

9. Rapid Alert System

This procedure covers the transmission of information when urgent action is required to protect public or health by means of a rapid alert relating to the recall of medicinal products, which have quality defects or which are falsified, the aim of the Rapid Alert System is to transmit only those alerts whose urgency and seriousness cannot permit any delay in transmission.

9.1 Criteria for Issuing a Rapid Alert

The urgency of the recall of defective medicinal products can be classified to:-
Class I defects are potentially life threatening. A rapid alert notification must be sent to all contacts of the rapid alert notification list irrespective of whether or not the batch was exported to that country. Transmission of a Class I rapid alert must be concurrent with the national action.

Class II defects could cause illness or mistreatment, but are not Class I. A rapid alert notification should be sent to all contacts of the rapid alert notification list as it might be difficult to know where a batch has been distributed. If the product distribution is known, the notification should be only sent to the contacts concerned. Whenever feasible, transmission of a Class II rapid alert should be concurrent with the national action but in all cases should be within 24 hours of the national notification. Class III defects May not pose a significant hazard to health, but withdrawal may be initiated for other reasons. These are not normally notified through the Rapid Alert System. The contact list for rapid alert notifications shall be only used for the transmission of notification falling in the scope of this procedure and the GMP non-compliance procedure; these messages should clearly identify the subject and whether they are for information or action.

All procedures should be documented and maintained up to date.

Contact lists for officials and companies should be maintained up-to-date and should be verified at intervals (e.g., a rolling program of annual checks of company contacts, possibly as part of GMP inspections).

All staff who could be involved in receiving a report of a suspected defective product or handling a Rapid Alert should be trained in the relevant procedures and have access to a copy of the SOPs and report forms wherever they needed.

9.2 Procedure for Rapid Alert

As soon as the product/batch (es) to be recalled is/are identified, licensee or representative of licensee or QA in charge shall review the information related to the defective product/batch (es) and decide about recall as per the procedure established.

The decision on recall of the defective product/batch shall be made within 24 Hours up to maximum of 72 Hours for Class I recall upon receipt of the intimation.



Within 24 Hours of the decision taken for the recall of the product/batch (es) the communication shall be sent stating the severity of the defect, using the fastest mode of communication which may include email, telephone, fax, SMS etc. to the entire supply chain.

The department from which the recall has been initiated will submit a recall alert within one working day after recall decision taken by the department recall Coordinator (DRC)

DRC should offer guidance to the recalling firm and will offer to review the text of recall communications to consignees so that the product will be promptly removed or corrected

Recall communications can be in multiple forms including press releases, telephone calls, telegrams, telefaxes, mailgrams, or first class letters.

All recall communications should be written in accordance with the following guidelines: be brief and to the point; clearly identify the product(s) such as the product name, size, brand name, serial numbers(s), potency, dosage, type, model, lot number(s)

Recall communications should be sent in the most expeditious manner and commensurate with the hazard of the product being recalled, and, where appropriate, sent with proof of receipt (e.g., by certified mail). All communication methods related to the firm's recall should be documented accordingly.

The licensee/representative of licensee where the product is marketed shall inform the concerned regulatory authority where the product batch (es) in question was distributed immediately after the decision of recall has been taken. Further actions on recall will be undertaken according to class of recall.

10. Intervals for efficient recall system and rapid alert

This is done based on the category of risk involved

Class one recall: Notification is made within 24 hours, with a maximum of 72 hours. For a second class recall, the notification is made within 72 hours, and the recall process is executed with a maximum of 10 days. The third class recall is notified within 5 days, and the recall process is executed with a maximum of 30 days allowed.

11. Implementation of recall

11.1 Stepwise Recall Procedure:

Once the product / batch or batches to be recalled by the authority have been identified, the company that owns the product or the agent of the product must be informed immediately. The authority will form a committee from the competent departments in order to ascertain the extent of the commitment of all parties to the success of the recall process and review the extent to which the time plan is followed based on the recall category and determine any Weaknesses in the process, whether by communicating with the company that owns the product or the importing agent, as well as distribution companies and public and private pharmacies, and following up on the detailed steps in the recall process. Accordingly, a file is opened by the formed committee specifying all the information related to the process.

The company that owns the product or the agent of the recalled product must inform the Authority of the distribution of the product / batch as soon as he is notified of the recall.

The company that owns the product or the agent of the recalled product must review the information related to the defective product / batch or batches, enter the details in the "Recall Record" and assign a unique recall reference number that represents the serial number of the month and year in which the recall began.

Within 24 hours of the decision taken to retrieve the product / batch or batches, the company that owns the product or the agent of the product that has been recalled or the head of quality in charge must inform the distribution company or the store by the fastest communication method which may include email, phone, fax, SMS etc. To stop the further distribution of the preparation and to reserve the quantities they have, depending on the severity of the defect that must be mentioned

The “Product/Batch Withdrawal Notice” must be filled out and sent by the company that owns the product, the agent for the recalled product, or the responsible head of quality to the distributor.

After completing these steps, the company that owns the product must provide the Authority with copies of the “product withdrawal notice” explaining the seriousness of the defect and warning of the reservation of quantities at the distributors and the withdrawal of the product from the market for each of the distributors indicated in the distribution statement.

The Distributor shall immediately check the distribution history to identify the customers and warehouses in which the respective product/runs have been distributed and send copies of the recall notice to them for further necessary action. The head of the main store or the head of the sales sector must ensure that the circulation of the product has been stopped by reviewing the register and at the same time keeping the available stock.

All branches must send Return Notes with merchandise (if any) to the main store. All returned stocks must be sent to storage warehouses.

The head of the main store or the head of the sales sector ensure that he sends a periodic report to the owner of the product or the agent for the product with the stock available to them and the returns received from the branches.

Head of Main Store or Head of Sales segment should reconcile the stocks of recalled materials against the total quantity of materials received and fill in “Product Summary Report / Batch Recall”.



The copy is sent to the owner of the product or the agent for the product with the stock they have, and the returns received from the branches for review, taking the necessary action and preparing for receiving the recalled quantities. The copy is sent to the competent department of the Egyptian Drug Authority based on the nature of the recalled product in the quantities to be returned to the companies that own the product or the agent of the product, the receipt of the owner of the product or the agent of the returns is monitored.

The recall of the product / lot depending on the recall category must be completed within the specified time.

12. Review phase

12.1 Follow-up procedures for goods returned by the drug authority

The inspectors of the EDA make an inventory of all quantities returned from the distribution companies to the company that owns the product.

An inventory is made of all the quantities in the stores of the company that owns the product, and it is matched with the quantities returned from the distribution companies.

The stock of returned goods must be placed under 'quarantine' and stored separately under lock and key in a secure area until a decision is made by EDA inspectors

A final report is made by the drug authority explaining all the observations on the recall process, identifying strengths and weaknesses, and determining any corrective measures for the process, if any.



There are factors that help in evaluating the recall as 1-The date of production of the batch and the time period from its production until the publication of the publication 2- Likewise, the recalled product or batch is specific to the local market or hospitals 3- Product consumption rate 4- Quantities in the possession of the owner of the product or agent and in distribution companies and warehouses, as well as the quantities that were distributed to pharmacies when the recall publication was issued Summoning class and summoning level.

A date must be set for the destruction of all the quantities recalled by the owner of the product or the importer, no later than three months from the date of issuance of the recall letter or the voluntary recall request.

12.2 Follow-up procedures for the returned goods by the owner of the product

12.2.1 In case of class II

The follow-up procedure consists of checking the effectiveness of the recall, investigating the cause of the recall and remedial actions taken to prevent recurrence of the defect.

The Licensee / Licensee's Representative / Head of Quality Assurance shall monitor the recall of the product / lot to determine whether the recall is proceeding satisfactorily.

The stock of returned goods must be placed under 'quarantine' and stored separately under lock and key in a secure area until a further decision is made.

Where required, the Head of Quality Assurance at the manufacturing site must perform a physical examination of the recalled merchandise and collect samples of the returned merchandise for investigation to determine the root cause of a product quality defect.

Investigation of recovered lot(s) shall be conducted in accordance with Licensee's SOP, "Investigation of Non-Conformity" to identify the root cause of failure and initiate corrective and preventive actions. Impact assessment shall be conducted on other runs of the product concerned and extended to runs of other product(s), where applicable.

If the reason for recall proves to be a quality issue associated with any of the raw materials used, then traceability of that material in all products/runs must be determined through records to identify the batches/products in which the specified materials were used.

12.2.2 In the case of first class I recall.

Monitor relevant data, i.e., material, plant and lot number in each of them

Determine traceability of raw materials in different formulations and their functions.

List all raw materials with batch numbers and quantities used in those batches.

List all products with batch numbers and related quantities used in those batches.

Calculate the total quantity by adding up the individual quantities used in different products/batches.

Monitor the movement of materials to get a complete stock overview for that particular material in the factory and extract information about the total quantity received and the stock quantity.

The balance, if any, should be checked against the actual physical stock available. A plan must be made to make a random drawing based on this data to verify the effectiveness and safety of products or processes.

The decision to withdraw any affected batches, if necessary, should be made after evaluating the quality of the product.

Based on the results of the investigation, the Head of Quality Assurance / authorized representative shall instruct the distributor / marketing company in order to appropriately dispose of the batch(s) of returned merchandise in accordance with the regulations.



13. References:

1. The Pharmacy Practice Law 127/1955
2. Ministerial decree 540/2007
3. The WHO TRS for GMP Guidelines.
3. EMA/572454/2014 Rev 17 Compliance and Inspection
4. USFDA documents on recall.
5. The Guidelines on Recall & Rapid Alert System for Drugs including Biologicals and Vaccines.