GUIDELINES ON RECALL OF DEFECTIVE THERAPEUTIC GOODS

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Drug Regulatory Authority of Pakistan
Islamabad – Pakistan

1. HISTORY

The Document Revision History of these Guidelines is as under:-

Edition	Changes / Amendment	Effective Date
01	Initial document	17-11-2021
02	The responsibilities of stakeholders have been elaborated in the recall procedure to enhance effective communication. The requirements and differences between statutory and voluntary recall have been included.	10-08-2024

2. APPLICATION - Guidelines for Regulators & Industry

This document is applicable to therapeutic goods industry and supply chain, healthcare professionals, patients, sponsors of clinical trials, and regulatory field force for reporting, investigating, and recalling suspected defective therapeutic goods products. These guidelines are expected to be followed by the licensees (manufacturers, importers, distributors, retailers, and sponsors) for voluntary or statutory recall including investigational products during a clinical trial. These guidelines aim to provide recommendations and explain the procedures to be adopted by the DRAP and the Pharmaceutical Industry (Manufacturers & Importers for effective removal of defective therapeutic goods from the market that may cause harm to the consumer and to safeguard public and animal health.

3. PURPOSE

These guidelines aimed at providing recommendations on the procedures adopted by the DRAP and industry for:

i. Safeguard public health from hazards of substandard and falsified products
ii. Recall and removal of substandard and falsified (SF) products
iii. Define the classification and levels of recalls;
iv. Communication of alerts to all stakeholders including general public;

v. Ensure that in the event that a recall is necessary, it shall be carried in an effective and efficient way;

This guidance will also assist the therapeutic goods industry in handling of a product recall, understanding what information should be provided to the DRAP and how to inform the consumer about a product recall.

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4. INTRODUCTION

Drug Regulatory Authority of Pakistan (DRAP) is responsible for ensuring that therapeutic goods available in market meet the prescribed standards of quality, safety, and efficacy. When a therapeutic good is suspected of being potentially harmful to consumers due to its defective quality, safety, efficacy, a recall shall be issued, and it must be removed from the market. This guidance document summarizes the series of activities to be undertaken in an event of a necessary recall to carry out recall operations in an effective and efficient way.

Drug Regulatory Authority of Pakistan (DRAP) is mandated with post marketing surveillance under Section 4(c) of DRAP Act, 2012 and is responsible for evaluation, coordination and monitoring of safety, efficacy and quality of drugs, drugs recall and withdrawals through Division of Quality Assurance and Laboratory Testing (QA&LT). These guidelines are made in light of section 7 (t) of the DRAP Act, 2012, wherein the Authority develops, adopts, issues and enforce the standards and guidelines to ensure safety, efficacy and quality of therapeutic goods. Moreover, specific legal Provisions regarding recall of Therapeutic Goods under relevant rules include; for Drugs and Biological products – Rule 3.7.1 of the Drugs (Licensing, Registering & Advertising) Rules 1976, for Medical Devices and Medicated Cosmetics – Rule 49(1) of the Medical Device Rules 2017 and for Nutraceutical products and Alternative medicines - clause (c) and (d) of Form-6 issued under rule 7(16) of the Alternative Medicines and Health Products (Enlistment) Rules, 2014.

This document will help both regulators and industry in setting up and maintaining a system that will enable the rapid and, so far as practicable, complete recall of any lot or batch of a defective therapeutic goods or Substandard and Falsified product from market, when an action is required to protect public or animal health. This document demonstrates stepwise procedures to be followed in recall execution and will also help in recall evaluation and achieving compliance within the stipulated time frame at every level. It is the responsibility of marketing authorization (registration/enlistment) holder to ensure that every level of supply chain (manufacturer, importer, distributor, and retail outlets) is well aware of the recall procedures.

GLOSSARY

Acronyms

ADR	Adverse Drug Reaction.
API	Active Pharmaceutical ingredient
AE	Adverse Event
BE&R	Biological Evaluation & Research Division
BMR	Batch Manufacturing Record
BPR	Batch Processing Record
cGMP	Current Good Manufacturing Practice
CSC	Clinical Study Committee
DRAP	Drug Regulatory Authority of Pakistan
DS	Drug Substance
EEC	Enlistment Evaluation Committee
FDA	Food and Drug Administration USA
FDP	Finished Drug Product
GRP	Good Regulatory Practices
H&OTC	Health & OTC Division
ICH	International Council for Harmonization
MA	Marketing Authorization
MDB	Medical Devices Board
MDMC	Medical Devices & Medicated Cosmetics Division
NRA	National Regulatory Authority
PE&R	Pharmaceutical Evaluation & Registration Division
PIC/s	Pharmaceutical Inspection Cooperation Scheme.
RB	Registration Board
RRA	Reference Regulatory Authority
WHO	World Health Organization

DEFINITIONS

Authentication	means self-checking of distribution history while accepting a shipment of therapeutic goods by the recipient (e.g., distributor, warehouse, hospital and institution or retailer) as is required to verify the distribution history.
Authorization	means permission granted by the DRAP to any legal person or owner(s) of company or firm to conduct manufacturing, import, export, sale or supply of therapeutic goods under the DRAP Act, 2012, The Drugs Act, 1976 and the rules framed thereunder.
Batch (or Lot)	means a defined quantity of starting material, packaging material, or finish product processed in a single process or series of processes so that it could be expected to be homogeneous in the case of continuous manufacture the batch must correspond to a defined fraction of the production, characterized by its intended homogeneity, and to complete certain stages of manufacture it may sometimes be necessary to divide a batch into a number of subbatches, which are later brought together to from a final homogeneous batch;
Batch No. (or Lot number)	means a distinctive combination of numbers and or letters which specifically identifies a batch on the labels, the batch records, the certificates of analysis, and that permit the production history of the batch to be traced and reviewed.
Batch Records / Batch Manufacturing Record (BMR)/ Batch Processing Record (BPR)	batch records mean all documents associated with the manufacture of a batch of bulk product or finished product showing a history of each batch of product and of all circumstances pertinent to the quality of the final product.
Board	means the concerned Board or any competent forum legally authorized under DRAP Act, 2012, The Drugs Act, 1976 and the rules framed thereunder.
Consignee	Anyone who received, purchased, or possesses the therapeutic goods being recalled.
Consumer / Users	Consumer / user is one who purchases therapeutic goods for its use. Consumer/user may include individual consumer, patients, physicians and hospital etc.
Customer	Any person, firm or party buying/receiving therapeutic goods from the company for storage, distribution and / or sale.
Defective Product	Attributes of therapeutic goods which may affect the quality, safety and/or efficacy of the product.

Distributor / Wholesaler	means a person / entity, buying the products for the purpose of selling again.
Drug	means drug as defined in Schedule-I of the DRAP Act, 2012.
Licensee	means manufacturer, importer, distributor, registration holder or enlistment holder of therapeutic goods.
Manufacture	manufacture means all operations of production, quality control, release, storage and the related controls.
Manufacturer	means a company that carries out at least one step of manufacture.
Marketing Authorization	means a document issued by the DRAP under the DRAP Act, 2012, as a certificate of registration / enlistment of a therapeutic good.
Pharmaceutical Product	means any drug intended for human use or veterinary use presented in its finished dosage form or as a starting material for use in such a dosage form.
Quality Control Laboratory (QCL)	means any laboratory notified for the test/analysis of therapeutic goods
Recall	means the removal of specific batch/batches of a therapeutic good/product from the market for reasons relating to the quality, safety or efficacy and/or if they are not in line with the particulars provided in registration / enlistment application of the product
Reference Regulatory Authority	means a regulatory authority as notified by any competent forum, board or committee of DRAP for the purpose of reliance.
Distribution / Wholesale	means sale to a person / entity, buying the products for the purpose of selling again
Retail Sale	means a sale other than distribution / wholesale.
Statutory Recall	A recall directed by the Drug Regulatory Authority of Pakistan (DRAP) / provincial government after notifying that product is considered to be in violation of the laws, the DRAP Act, 2012, The Drugs Act, 1976 and the rules framed thereunder.
Substandard and Falsified (SF) Products	Substandard drug means a drug as defined in Section 3 (zz) of the Drugs Act, 1976. Whereas Falsified products include Spurious, Adulterated, Misbranded and Counterfeit drugs (as defined in Section 3 (zb), 3 (a), 3 (s) and 3 (f) of the Drugs Act 1976 respectively).

Supply chain	means transfer of ownership of API i.e. the upstream supply chain (sources and path of ingredients that go to the manufacturer) and the product i.e. downstream supply chain (path of the finished product after it leaves the manufacturer) for each requirement regarding pedigrees / transaction records, authentication / verification.
Therapeutic Goods	includes drugs or alternative medicine or medical devices or biologicals or other related products as may be notified by the Authority under Section 2(xxxvi) of the DRAP Act, 2012. (Therapeutic goods may hereinafter refer as the product.)
Voluntary Recall	A recall initiated by the manufacturer as a result of unusual observation in any product's quality during periodic review (Internal / External) or investigation of a market complaint or any other failure or otherwise, is defective that present a risk of injury to human / animal.

5. RECALL PROCEDURE

DRAP is responsible for oversight of recall and the purpose of a recall is to protect patients and consumers from any potential harm that may be caused by use of a defective therapeutic goods. A defective therapeutic good is one that is suspected to be harmful under normal conditions of use or that does not comply with its marketing authorization (as its registered) specification or that is lacking in therapeutic efficacy or that has not been manufactured in accordance with accepted standards of Good Manufacturing Practice (GMP). The Registration / Marketing Authorization holder is primarily responsible to carry out complete recall whether voluntary or statutory.

In almost all cases, a product recall can be divided into following five stages: -

i. Receipt of Information of Defective Product (Problem Report)
ii. Submission of Information for Assessment of a Recall
iii. Assessment of Recall
iv. Recall communication to remove defective products from market
v. Monitoring and Evaluation of Recall

5.1. Receipt of Information of Defective Product (Problem Report)

There are several means for receipt of information that trigger the initiation of Recall process. A recall might be initiated voluntarily by the licensee or statutorily by DRAP or Provincial Drug Control department. In case of a statutory recall, the information received by the Office of Substandard and Falsified (SF) handling and Product Recall oversight may be from a National Quality Control Laboratory in the form of a test/analysis report OR a complaint from general public or a manufacturer/importer that ultimately leads to the generation of out of specification test/analysis report. DRAP or the Provincial Health departments can order a statutory recall of a product to the licensee upon receipt of defective product report. The reports or complaints leading to a statutory recall may be generated by the following means:

i. Healthcare professionals, physicians, pharmacist, dentists, and patients.
ii. Test/analysis report of products by the National or Provincial Quality Control Laboratories.
iii. Recall of products by principal manufacturer abroad or by the overseas National Regulatory Authorities or from information received directly from other NRAs or WHO;

iv. Hospitals or Research institutes;

v. Manufacturers or distributors or wholesalers or pharmacies or drug sale outlets (retailers).

Fig.(i) below explains the sources of trigger information of a defective therapeutic good or any substandard and falsified product.

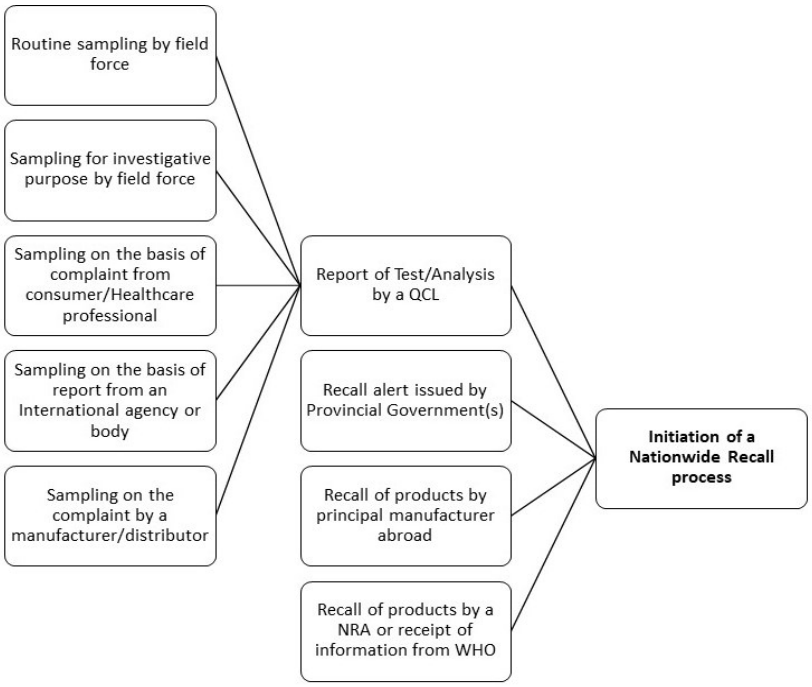


Figure 1 Receipt of Trigger Information and Initiation of Recall Process

Upon receipt of information from DRAP/Provincial Health department, the licensee will analyze the information and immediately initiate the recall of product in question following the procedure provided in these guidelines.

5.1.1. Action Group on Risk Assessment and Recall of SF Products

The Action Group on Risk Assessment and Recall of SF products is a collaborative working group of DRAP and all federating Units and is responsible for regulatory oversight of recall in the country. The Action Group with the support of office of SF handling and Product Recall Oversight, Division of Quality Assurance and Lab Testing DRAP, performs following functions:-

a. Receiving and assessing reports of suspected defective therapeutic goods.

b. Determination of class of recall, level of recall, and devise a strategy for effective recall.

c. Assessment and identification whether the product is imported, locally produced or

locally produced and exported.

d. Advising and monitoring necessary actions by the relevant licensee.

e. Communicating the details of actions to be executed by the relevant stakeholders.

f. Recommendations to the relevant Board or Committee on appropriate action.

g. Monitor the effectiveness of recall and recommend follow up actions.

h. Share information to National Focal Points for reporting to WHO Global Surveillance and Monitoring System (GSMS)

The Action Group will achieve these goals and classify the risk by assessing the health hazard associated with the type of defect. Action group will utilize various means for communication and coordination which include any electronic means such as E-mail or WhatsApp etc. For the said purpose, following parameters can be taken in consideration:

i. Whether any disease or injuries have already occurred from the use of the product.

ii. Whether any existing conditions could contribute to a clinical situation that could expose humans or animals to a health hazard. Any conclusion shall be supported as completely as possible by scientific documentation and/or statements that the conclusion is the opinion of the individual(s) making the health hazard determination.

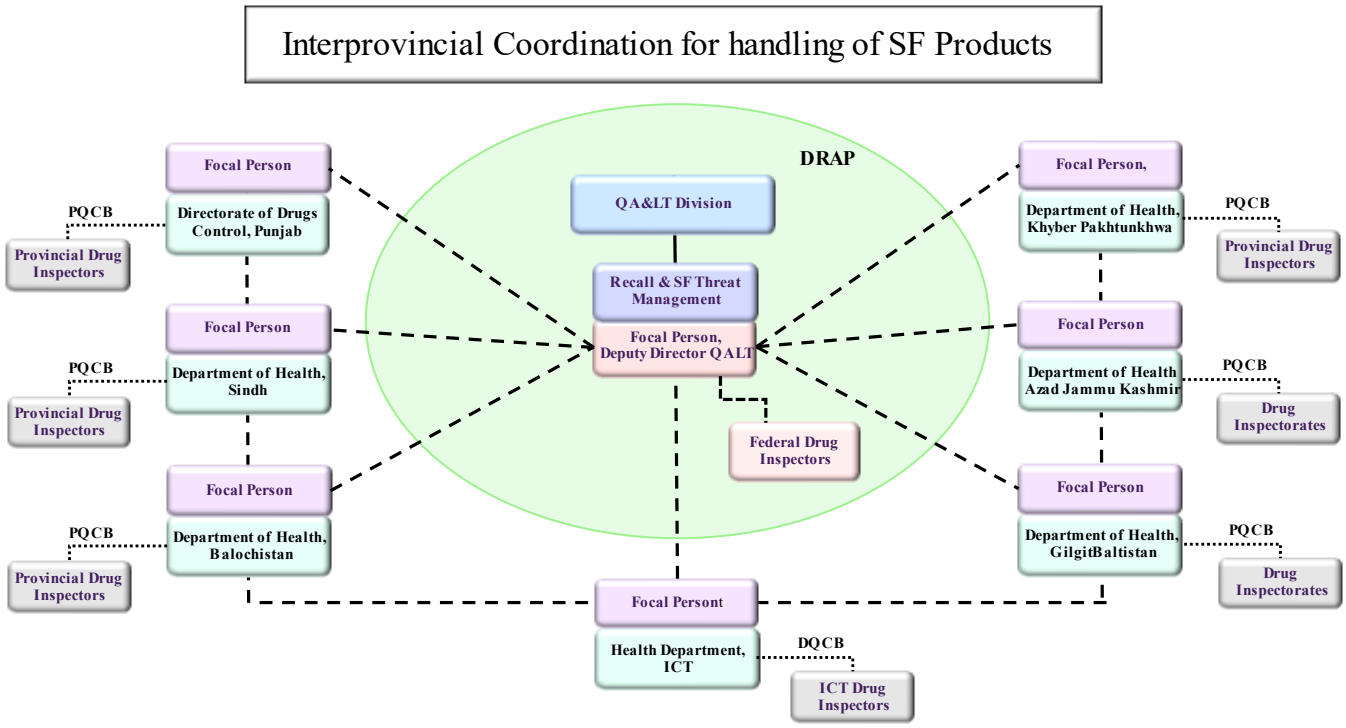
iii. Assessment of hazard to various segments of the population, e.g., children, surgical patients, pets, livestock, etc., who are expected to be exposed to the product being considered, with particular attention paid to the hazard to those individuals who may be at greatest risk.

iv. Assessment of the degree of seriousness of the health hazard to which the populations at risk would be exposed.

v. Assessment of the likelihood of occurrence of the hazard.

vi. Assessment of the consequences (immediate or long-range) of occurrence of the hazard

Based on these factors, the action group will ascertain the recall classification to indicate the relative degree of health hazard of the product being recalled or considered for recall and propose a recall strategy.



5.2 Submission of Information for Assessment of a Recall

When a licensee initiates a recall of a product, they are required to notify DRAP about the recall situations, and all relevant information required for the assessment of recall on the Recall Assessment Form (**Annexure-I**). The information provided on Annexure-I should be complete in all aspects and provided in defined timelines, appropriately signed and stamped by person nominated as focal person for recalls by the licensee. The information required for assessment of a recall generally includes following three categories:

a) *Details of the Problem*

i. Name and contact of the person reporting problem;
ii. Date of problem reported;
iii. Problem location;
iv. Problem nature or type of defects in product;
v. Any similar problem reports;
vi. Results of quality control tests and other investigations on suspected or other samples.

b) *Details of the Product(s)*

i. Proprietary (brand) name of product, dosage form, strength and active ingredients;
ii. Registration / enlistment number and pack size details;
iii. Batch number(s), quantity, manufacturing and expiry date;
iv. Manufacturer / importer name with contact details and local distribution list;
v. If the product was exported, then also provide detail of importing country(ies);

c) Risk Assessment and Proposed Action by Licensee

i. Assessment and evaluation of potential hazard to consumer;
ii. Proposed action;
iii. Proposed recall classification and level; and
iv. Availability of alternative product.

5.2.1. Recall Classification

Recall classification is a numerical designation, I, II, or III that is assigned to a particular recall. This classification indicates the relative degree of health hazard presented by the product being recalled and determined by regulatory authority(ies). Details of these classes are given as under:

Class	Risk Classification	Examples
Class I	The defect presents a **risk of death or disability**.	• Wrong product (label and contents are different products) • Correct product but wrong strength, with serious medical consequences. • Microbial contamination/any foreign particle visible with naked eye in a sterile injectable of sterile injectable or ophthalmic product. • Chemical contamination with serious medical consequences. • Mix up of products (‘rogues‘) within a pack. For example, two different blister strips within one outer carton, or, two different tablets within the one blister strip. • Wrong active ingredient in a multi-component product with serious medical consequences. • Serious adverse reactions which are batch or product related. • Any other situation as the Competent Authority or the Board may consider.
Class II	The defect may cause mistreatment or harm to the patient and may cause	• Mis-labelling - wrong or missing text or figures. • Missing or incorrect information - leaflets or

	temporary or medically reversible adverse health consequences, that are not life-threatening.	inserts. • Microbial contamination of non-injectable, non-ophthalmic sterile product with medical consequences. • Chemical/physical contamination (significant impurities, cross-contamination, particulates). • Mix up of products. For example, a case of product A contains one or more packs of product B. • Non-compliance with specification (e.g. assay, dissolution, stability, content uniformity, fill/weight). • Insecure closure with serious medical consequences (e.g. cytotoxic, child-resistant containers, potent product). • Any other situation as the Competent Authority or the Board may consider.
Class III	The defect is **unlikely to cause harm to the patient**, and the recall is carried out for other reasons, such as non-compliance with the marketing authorization or specification.	• Faulty packaging - for example, wrong or missing batch number or expiry date. • Any other situation as the Competent Authority or the Board may consider.
Class IV	These are known as "Medical product notifications" and in these scenarios, DRAP issues "Caution in Use" notices, where there is no threat to patients or no serious defect likely to impair product use or efficacy.	• These are generally used for minor defects in packaging or other printed materials. "Caution in Use" notices may also be issued where a defect has been identified but due to supply concerns product cannot be recalled, in these instances the alert will be used to provide advice to healthcare professionals.

5.2.2. Levels of Recall / Depth of Recall

The level (or depth) of recall of a product/batch shall be determined based on the level to which distribution of the product in question has taken place. The levels of recall are given as under:

Level of recall	Details
Consumer / User level	Consumer or user level may include individual consumers, patients, physicians and hospitals.
Retail level	Recall to the level immediately preceding consumer or user level. It includes retail groceries, pharmacies, hospital pharmacies,

	dispensing physician, institutions such as clinics and nursing homes, etc.
Distributor / wholesale level	This includes all distribution/wholesale levels between the manufacturer and / or importer and retailer.

5.2.3 Timelines for Effective Recall System

Based on the category of risks involved, timelines are defined. The timelines defined are for initiation of recall procedure to commence from the receipt of information as notified by the Drug Regulatory Authority of Pakistan (DRAP) under statutory recall or voluntary recall by the manufacturer on its own. Details are given as under:

Class of Recall	Initiation Time (From time of identification of defect)	Time to ensure Physical Recall from initiation
I	<48 hours	Max 7 Days
II	< 48 - max 72 hours	Max 21 days
III	< 48 - max 72 hours	Max 30 days
IV (Caution in use notice)	< 48 – max 72 hours	N/A

5.2.4. Recall Strategy

As the information related to the defective therapeutic goods start assembling, the licensee will devise and discuss the proposed recall strategy and recall classification with the Action Group on risk assessment and recall of SF products through the office of SF handling and Product Recall oversight. Any factors which may affect the duration of recall shall also be informed by the licensee. The proposed recall strategy should be agreed by the action group before implementation. The actual implementation of the recall includes use of the basic steps which are summarized below and these will be common to all strategies:

i. Indicate the proposed level in the distribution chain to which the recall is extending, if the recall only extends to the wholesale level, the rationale of not recalling to retail level should be explained;

ii. In case of consumer level recall, additional information such as list of point of sale etc. should also be provided

iii. Indicate the method of notification (e.g. phone, email etc.);

iv. Indicate how the message of recall will be delivered to customers e.g. press release or recall letters etc. and if the Licensee has a website, it should consider posting the recall notification on it as an additional method of recall notification;

v. Report on what have the customers been instructed to do with the recalled product;

vi. 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;

vii. If product is to be returned, explain the mechanics of the process;

viii. Explain if the recall will create a market shortage that will impact on the consumer.

5.2.5. Difference between a Voluntary and Statutory recall

Voluntary recall is initiated by the manufacturer as a result of unusual observation in any product's quality during periodic review (Internal / External) or investigation of a market complaint or any other failure or otherwise, is defective that present a risk of injury to human / animal. In case on a Voluntary recall, the licensee is bound to inform DRAP regarding the details of recall including; type of problem identified in the product, source of complaint, details of product (Brand name, Generic name, Strength, Pack size, Batch No., Mfg. Date, Exp. Date, Batch size and list of distributors), and action initiated so far. All of the stated information should be provided keeping in view the timelines and procedures explained further in these guidelines. DRAP will issue recall notice to the firm wherein requiring the firm to provide any other information required and monitor the progress of recall. In case a voluntary recall is assessed to be a statutory recall, the Action group will modify the classification and proceed with it as a statutory recall.

Statutory recall is directed by the Drug Regulatory Authority of Pakistan (DRAP) / Provincial Government after notifying that product is considered to be in violation of the laws, the DRAP Act, 2012, The Drugs Act, 1976 and the rules framed there under. For a statutory recall, the procedure will be adopted as explained above.

5.3 Assessment of Recall

The licensee will submit an initial report to DRAP following the timelines provided in this document. Action group on risk assessment and recall of SF products will assess the information

provided by the firm and information provided by the QCL (in case of statutory recall) and will finalize the Class of recall, Level of recall and devise a strategy for recall process. This information will then be shared with the licensee to ensure the effective implementation of recall strategy. Provided below are the details of classification of recall, level of recall and the recall strategy.

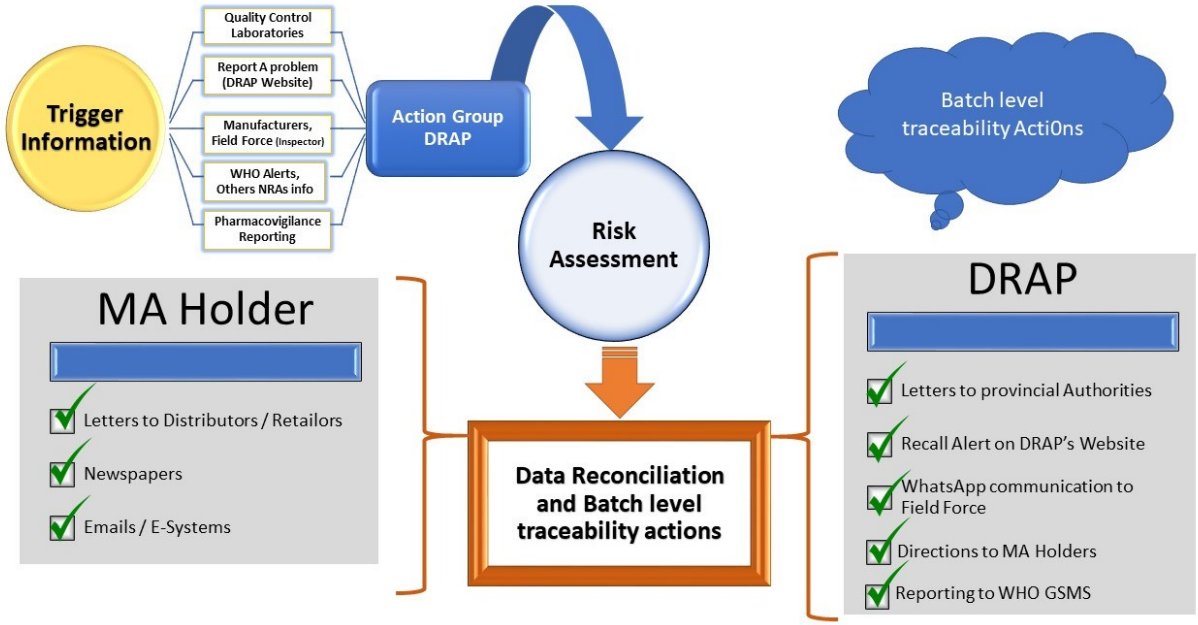


Figure 1: Recall Assessment, Risk Communication and Data Reconciliation

5.4 Recall Communication to Remove Defective Products from Market

5.4.1 Methods of Communication to be adopted (Communication channels)

DRAP and the licensee both will communicate the recall alert/notices to their respective stakeholders. DRAP will issue recall alert/letters to the manufacturer and recall alerts for Provincial Drug Control departments, healthcare professionals and general public. For this purpose DRAP can adopt any means of communication like print media (if required), social media and DRAP's official website. The licensee will adopt best approaches for effective communication of recall alert/letter to the targeted audience which include letters to distributors/point of sales and public notices in print media. Following methods are to be adopted by manufacturer and DRAP for effective communication:

Communication Method	Recall Classification
• Recall letters/Notices (by both DRAP and Licensee)	Class I, Class II and III
• Press Release (only by licensee)	Class I or Class II (to be decided by the action group)
• "Caution in use" notice (only by DRAP)	Class IV only

5.4.2 Recall letters

Recall alert/letters are most commonly used tool for effective communication by the licensee with the distribution network, pharmacies/retail outlets and healthcare professionals. In case of a statutory recall, DRAP will issue a recall alert/letter to the licensee, informing them regarding the problem identified in the product and directing them to recall the defective product from the market. In response, the licensee will issue a recall alert/letter throughout its supply chain for effective recall of the defective product. However, in case of a voluntary recall, the initial information is issued by the licensee throughout its supply chain and DRAP. A recall alert/letter must be on the licensee's letterhead containing comprehensive information including a factual statement for the reason of recall together with the specific details to allow easy identification of products. Recall letter should also include issuing date and signature along with title and name of signatory. A specimen recall letters is provided at **Annexure-III.**

The recall letter may be sent by email, or other appropriate electronic communication channels (WhatsApp etc.), or by post. A recall letter may include

i. **Description of the Product:** Brand Name; DRAP Registration/Enlistment Number; Name of Registration/Marketing Authorization holder; Name of manufacturer; Pack size; Dosage form; Batch number(s) and Expiry date.

ii. **Reason for Recall:** 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. **Contact Details:** The Licensee should clearly identify a helpline for enquiry.

5.4.3 Press Release

Press releases are responsibility of the licensee and are issued to public for mass disseminating

information of hazards categorized as Class I and where appropriate, Class II.

5.5. Progress Monitoring, Evaluation of Recall and Follow Up Actions

5.5.1 Responsibilities of Licensee and role of management

Licensee has the prime responsibility for implementing recall action and for ensuring compliance with the recall procedure. The licensee is responsible to develop an effective recall system and maintain all records which will assist in recalling a product from the market.

Generally, 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 later.

Licensee is also required to retain records of complaint received about each product. Complaints should be examined appropriately by the nominated technical person/team and any subsequent action taken should also be documented and shown in the records.

To check the effectiveness of recall system, Mock recall shall be carried out for at least one batch of any product that is dispatched for sale where maximum distributors are involved. During mock recall traceability shall be performed for at least, one of the raw materials used in the batches identified for mock recall. Records of such mock recall shall be maintained by the QA Head of the Licensee or any designated person and presented to Drug Inspector when required/inquired.

Following are the general responsibilities amongst the management of licensee:

Management Position	Responsibility
Director/CEO	• To monitor and ensure effective recall.
QC/QA Head	• Informing the management in writing about any product defect which may require recall. • Informing the regulatory authorities immediately after recall decision is made. • Issuance of recall notice to all distributor/ marketing company. • Overseeing the system for receiving, verification, quarantining, segregation and securing of recalled stock. • Labelling of the recalled stock. • Investigating the incident which resulted in a product recall. • Making decision on destruction /disposition of recalled stock as per SOP of the firm.

Warehouse Head	• Receipt, verification, quarantine/ segregation and secured storage of recalled stock under lock & key. • Informing QC/QA about the recalled goods. • Providing support during recall investigation.
Distributor/Marketer	• Ensure the removal of defective batch of product from the market in a stipulated time as per class of the recall. • Co-ordinate with Wholesalers / retailers for the recall of batch(es) in the market.
Wholesalers/Retailers	• To hold the defective batch(es) of product immediately after the receipt of the recall information. • Co-ordinate with consumers for the recall of batch(es) in the market.

5.5.2 Recall Reconciliation Report

After the completion of timeframe of recalling product, or at other agreed intervals in accordance to the directions of the Action Group, the licensee shall submit interim and final report to monitor the progress of recall implementation.

5.5.3 Interim Report

The interim report shall be submitted to Action Group as soon as possible from the commencement of recall while keeping in mind the timelines defined according to the class of recall. The interim report shall consist at least following details:

i. Reason of recall;
ii. When the recall notification was issued, and which communication channels were utilized.
iii. Number of distributors/firms/institutions etc., whom the defective product(s) was supplied;
iv. Number of responses received from them;
v. Names of entities which did not responded to licensee for recall notification;
vi. Quantity of stock returned till report date;
vii. Estimated time frame for the completion of the recall.

5.5.4 Final Report

A final report should be submitted to Action Group within the defined timeline and following information should be provided in the final report:

i. Reason for recall;
ii. Details of Actions taken by the Licensee;

iii. Extent of distribution of the relevant batch across the country and export
iv. Quantity of stock returned, corrected, outstanding;
v. Quantity of stock consumed;
vi. Quantity of stock not located;
vii. Date of recall completion;

5.5.6 Evaluation & Monitoring of the Recall

The purpose of evaluation is to check effectiveness and verify that all consignees at the recall depth specified by the strategy have received notification about the recall and have taken appropriate actions for removal of defective product. The recalling firm will be responsible for conducting effectiveness checks and will include these in the final report submitted to DRAP.

In addition to the effectiveness checks conducted by recalling firm, DRAP itself or through its field offices, may also contact or inquire firm's customers as a means of assuring that the recalling firm and its consignees are performing their recall responsibilities. If DRAP determines the recall to be ineffective, the recalling firm will be asked to take appropriate actions, including re-issuing recall notifications.

5.5.7 Follow-Up Actions

The follow-up action may consist of a check on the effectiveness of a recall, an investigation of the reason for the recall, root cause analysis and remedial action taken to prevent recurrence of the defect.

The licensee/representative of licensee/QA Head of licensee shall monitor the recall process of product/batch to determine whether the recall is progressing satisfactorily.

The stocks of recalled goods shall be placed under “Recall goods area” and stored separately under lock and key in a secure area until final decision.

Wherever required, QA head of the licensee shall perform the physical inspection of recalled goods and collect sample from recalled goods for investigation to establish the root cause of the product quality defect.

The investigation of the recalled batch(es) shall be conducted as per the SOP of the licensee, on “Investigation of Non-conformities” to identify the root cause of the failure and initiate corrective

and preventive actions (CAPA).

Impact assessment shall be conducted on other batches of the concerned product and further extended to batch(es) of other product(s), wherever applicable.

If the cause of recall is established to be quality issue associated with any of the raw material used, then the traceability of that material shall be established in all the product(s)/batches.

Based on conclusion of the investigation findings, the QA Head of licensee / representative of licensee shall forward investigation report along with corrective and preventive action and appropriate disposition plan of the batch(es) of recalled goods as per destruction/disposition SOP of licensee to the Directorate of QA&LT, DRAP. Disposition/destruction shall be done in the presence of Drug Inspector or a team specified for the purpose by DRAP.

5.5.8 Recall Closure

A recall will be closed when Action Group determines that all reasonable efforts have been made to remove or correct the product in accordance with the recall strategy, and when it is reasonable to assume that the product subject to the recall has been removed and proper disposition or correction has been made according to the degree of hazard of the recalled product. Written notification that a recall is terminated will be issued by QA&LT Division of Drug Regulatory Authority of Pakistan to the recalling firm.

6. RESPONSIBILITIES OF STAKEHOLDERS IN NATIONAL REGULATORY SYSTEM

6.1 Responsibilities of the Drug Regulatory Authority of Pakistan

To execute an effective Nationwide recall, following functions are to be performed by the Drug Regulatory Authority of Pakistan:

i. Issuance of Recall notice to licensee and forward a copy of same to the Provincial Drug Control Departments. Same will be shared with the National Task force to ensure the effective monitoring of the recall. If required, the same will also be shared with International NRAs /Foreign Government/ Authorities (in case of an imported or exported medicinal product).

ii. Issue Recall and Rapid alerts for the information of regulatory field force, medical health

professionals and general public on DRAP's official website: www.dra.gov.pk

iii. On receipt of recall information by the firm, Action group for Risk assessment and recall of SF products reviews the information and recall strategy provided by the firm and suggests changes, if required.

iv. When a firm refuse to recall after being requested or ordered to do so by the Authority or the Authority has reason to believe that the firm's recall strategy is not effective, or is not being implemented effectively, Regulatory actions will be taken as recommended by Director QA&LT or the Action Group or by the relevant Board for the purpose.

v. The role of the inspectorate of QA&LT Division in collaboration with the Provincial Health Departments and National Task Force is to verify the adequacy of the Licensee's actions on the recall of the product and to monitor the progress and effectiveness of the recall till appropriate disposal of recalled product is achieved.

vi. For verification of root cause of the deviation in the product identified by the licensee and Corrective action / preventative action, concerned Board may recommend an establishment inspection of the licensee by Federal Inspector of Drugs or a panel of experts (which may include Federal Inspector of Drugs) which may be followed by sampling of recalled product, if required.

vii. It is also role of DRAP to ensure that product recall is not used as promotional means by any manufacturer/importer and such action shall be deemed as contravention of conditions of advertisement.

viii. DRAP will issue recall notice/letter and recall alert based on information received from or a recall initiated by any Provincial Health Department. Office of SF handling and Product Recall oversight in coordination with Action group on risk assessment and recall of SF products, National task force and Provincial Drug Control Departments will monitor the progress of recall till closure of recall.

6.2 Responsibilities of Provincial Drug Control Departments

i. Provincial Health Control departments will forward information regarding initiation of recall to DRAP through communication means such as letters, E-mail or WhatsApp etc.

ii. Provincial Government will conduct market surveillance in coordination with National Task Force to ensure the effective removal of defective product from the market.

iii. In case of presence of defective product found at any distribution, point of sale or any other health facility (Hospital or Clinic), the field force of Provincial Drug Control Department

will seize the available stocks and report to office of SF handling and Product Recall oversight, Division of QA&LT DRAP immediately.

6.3 Responsibilities of Quality Control Laboratories

i. Laboratories working under the administrative control Federal Government i.e. Central Drugs Laboratory Karachi and National Control Laboratory for Biologicals Islamabad will directly share their reports of any defective product with SF handling cell of the Drug Regulatory Authority of Pakistan.
ii. Laboratories working under the administrative control of Provincial Health Departments (Provincial Drug Testing Laboratories) will share the information/report of any defective product with the office of SF handling and Product Recall oversight, Division of QA&LT DRAP directly or through their concerned Quality Control Board or any other mechanism as may be prescribed.

6.4 Responsibilities of Action Group on Risk Assessment and Recall of SF Products

i. Receiving and assessing the reports of suspected defective therapeutic goods from Quality Control Laboratories (through office of SF handling and Product Recall oversight, division of QA&LT DRAP).
ii. Determination of class of recall, level of recall, and devising a strategy for effective recall.
iii. Advising and monitoring necessary actions taken by the relevant licensee.
iv. Communicating the details of actions to be executed by the relevant stakeholders i.e. Provincial Drug Control Departments, National Task Force and office of SF handling and Product Recall oversight.
v. Recommendations to the relevant Board or Committee on appropriate action.
vi. Monitor the effectiveness of recall and recommend follow up actions to the licensee and other stakeholders.

6.5 Responsibilities of Office of Substandard Falsified (SF) handling and Product Recall Oversight

i. Issuance of Recall notice to licensee and forward a copy of same to the Provincial Drug Control Departments. Same will be shared with the National Task force to ensure the effective execution of the recall. If required, the same will also be shared with Foreign

Government/Authorities (in case of an imported or exported medicinal product).

ii. Issue Recall and Rapid alerts for the information of regulatory field force, medical health professionals and general public on DRAP's official website: www.dra.gov.pk

iii. When a firm refuse to recall after being requested or ordered to do so by the Authority or the Authority has reason to believe that the firm's recall strategy is not effective, or is not being implemented effectively, office of SF handling and Product Recall oversight will process the matter and recommend regulatory actions to be taken to through the Director QA&LT to the relevant Board.

iv. Office of SF handling and Product Recall oversight will issue recall notice/letter and recall alert based on information received from or a recall initiated by any Provincial Health Department. Office of SF handling and Product Recall oversight in coordination with Action Group on risk assessment and recall of SF products, National task force and Provincial Drug Control Departments will monitor the progress of recall till closure of recall.

6.6 Responsibilities of National Task Force (NTF)

i. The National Task Force (NTF) will conduct market surveys based on the information shared by the office of SF handling and Product Recall oversight regarding the presence of falsified products in the market and report the findings in a timely manner.

ii. On receipt of information regarding a product recall (statutory or voluntary), National Task Force (NTF) will facilitate the execution of a successful recall by conducting market surveys at the point of sales (POS) and distributors in their respective area of jurisdiction and report to the office of SF handling and Product Recall oversight.

iii. Members of the National Task Force (NTF) will respond and report on the complaints related to their respective area of jurisdiction shared by DRAP or any Provincial Drug Control administration.

iv. Members of the National Task Force (NTF) will submit their activity report to the office of SF handling and Product Recall oversight by any mean of communication defined by the said office.

7. REFERENCES

In developing these guidelines, guidance documents referred are;

i. The Drugs Act, 1976.
ii. DRAP Act 2012.
iii. PIC/S Procedure for Handling Rapid Alerts and Recalls Arising from Quality Defects - PI 010-5 – 1 July, 2017 (https://picscheme.org/docview/2681)
iv. TRS 986 - Annex 2: WHO good manufacturing practices for pharmaceutical products: Main principles
v. A Guide to Defective Medicinal Products 2021 – MHRA UK (https://assets.publishing.service.gov.uk/media/6103ba7a8fa8f5042c338d1c/DMRC_Guide-to-Defective-Medicinal_Products-Aug2021.pdf)
vi. Regulatory Procedures Manual 2021, Chapter 7: RECALL PROCEDURES, US-FDA. (https://www.fda.gov/media/71814/download)

ANNEXURE-I

Recall Assessment Form

(To be filled by Licensee on their letterhead)

To, Recall Ref. No. _____

Date: _____

Recall information	Information provided by Licensee	Comments of Action group on Risk Assessment and Recall of SF Products (For DRAP use only)
Origin of report		
Name of person/organization reporting the problem(State whether it is a complaint, quality defect, lab report, voluntary or statutory)		
Date of report		
Name of recalling firm		
Physical address of recalling firm		
Telephone number of recalling firm		
Alternate number of recalling firm		
E-mail address of recalling firm		
Name of nominated person of recalling firm		
Product(medicine) details		
Name of product affected		
Registration number		
Dosage form		
Strength		
Pack size/type		
Batch number(s) and expiry date		
Date manufactured		
Date released		
Total quantity prior to distribution		
Quantity released for distribution prior to the recall		
Date of distribution (Annex list of distributors along with date of distribution – Provide separate list for local and overseas distribution)		
Nature of defect		
Source of problem		
Details of problem		
Number of complaints received (if		

any)		
Action taken so far (if any)/ Proposed action and its urgency		
Type of hazard/health risk and assessment of risk to the user		
Proposed recall classification and level of recall		
Other relevant information		

*This form should be submitted to DRAP within the timelines prescribed in this document.

Signature of contact person
& Stamp of Licensee

ANNEXURE-II

RECALL LOG (RECONCILIATION FORM)

(To be filled by the Licensee on their letterhead)

Name of Manufacturer/Importer	
Contact person name and Phone number	
Recall Ref. No.	
Time and Date of Recall initiation	
Product name	
Batch/Lot No.	
Mfg. date	
Exp. Date	
Reason of recall	
Recall Classification (Proposed by licensee)	
Quantity Produced / Batch Size	
Undistributed quantity in possession	
Quantity Distributed	
Quantity Returned / Recalled	
%age of recall	
Remarks (If any)	

Signature of contact person
& Stamp of Licensee

ANNEXURE-III

SAMPLE RECALL LETTER TO BE ISSUED BY LICENSEE TO DISTRIBUTORS / MARKETING FIRM / RETAILS OUTLETS ETC.

(To be issued by Licensee on their letterhead)

To,

Recall Ref. No. _____

Date: _____

Please stop further distribution/sale of below mentioned product/batches with immediate effect. Kindly recall the stocks of these batch(es) from the market and return immediately.

Product Details (Name, Strength, Dosage form, Pack size, Reg. Enl. No.)	Batch/Lot No.	Mfg. Date	Exp. Date

Reason of Recall:

_____

Sign and Stamp of Licensee

DRUG REGULATORY AUTHORITY OF PAKISTAN
Prime Minister National Health Complex, Park Road,
Islamabad, Pakistan
Email: addl-dir.qa@dra.gov.pk Phone: +92-51-9255969
www.dra.gov.pk