

**“QUALITY SYSTEM” TO HANDLE COMPLAINT AND RECALL IN PHARMACEUTICALS: A REVIEW**\* Bhupender Kumar Nimbiwal<sup>1</sup>, Prof. Rajesh Kumar Dholpuria<sup>1</sup>, Ramchandra<sup>1</sup>, Monish Sharma<sup>1</sup>Department of Quality Assurance, Seth G. L. Bihani S. D. College of Technical Education, IPSDR, Sri Ganganagar, Rajasthan, India – 335001**ABSTRACT**

'Quality' means compliance with statutory or agreed standards rather than grade of materials and workmanship. Manufacturers use many controls to make sure that the products they produce are safe. Sometimes, for many different reasons, a product may be manufactured and sold which may make some people ill or injure them, or is in violation of the legislation. When an unsafe product has left the control of the manufacturer, after complaint products must be recall from the market. Good manufacturing practice ensures that products released for distribution are of the appropriate quality. Medicinal products are distributed to the general public without any alteration of their properties. "For those drugs for which environmental assessments have been required, there has been no indication of environmental effects due to flushing," says Bloom. Despite the safety reasons for flushing drugs, some people are questioning the practice because of concerns about trace levels of drug residues found in surface water, such as rivers and lakes, and in some community drinking water supplies. So allow the public to bring unused drugs to a central location for proper disposal.

**KEYWORDS:** Quality, Legislation, Good Manufacturing Practice, Complaint, Recall**INTRODUCTION****COMPLAINTS (AS PER INDIAN GMP):**

Guidelines recommend that a person should be designated for handling complaints and to decide the measures to be taken.

**Objective:** Objective of the guidelines under this element is that a defective product is immediately recalled, matter is investigated & remedial measures are taken.

All verbal or written complaints or reports received by the manufacturer are complaints. Complaints may be of three types **Quality complaints** usually originate at consumer level and concern with physical, chemical and biological properties or condition of labeling and/or packaging of the product. **Adverse drug reaction (ADR)** may be allergic reactions or any other untoward reaction or fatal reaction or near fatal reaction. **Other medically related complaints** include complaints such a lack of efficacy or clinical response <sup>[1]</sup>.

**COMPLAINT FILES:** There are three main parts to the complaint file:

- Recording of the initial complaint information
- Investigation at your storage facility
- Action taken for the specific product <sup>[2]</sup>

**HANDLING OF COMPLAINTS: AS PER INDIAN GMP:**

A written record should be maintained for all complaints received. The quality complaints should be forward to the quality control department of the

manufacturing unit. Report of adverse reaction should be a member of this committee. Usually the Medical Advisor of the company is the competent person to handle ADR.

Upon receipt of complaints, quality control unit should review all the incoming information. If a sample has been received along with complaint, the sample should be examined and tested. If need be, retained reference sample should be examined, tested/analyzed. All the relating data and documentation should be reviewed. When investigation is complete, conclusion on the cause and action should be reported to the management. If it has been found out that the complaint is the result of defective production then a copy of completed report should be sent to the production department to take corrective action. If formulation or process of manufacture is required to be amend. Master formulation record should be amended accordingly and should be authorized. If it is found, on investigation, that the complaint is result of defective, ingredients or packaging materials, a copy of report should be sent to the purchasing unit for corrective action. It may also be examined whether any other batch (es) should be recalled. It is the responsibility of the In-charge, Quality control to see that each complaint is recorded, evaluated and reported to the management. <sup>[1]</sup>

**RECORDS: AS PER INDIAN GMP AND ICH:** Records of complaints should include the following information:

**CONTENTS OF COMPLAINT:**

These should include:

- Name, dosage form, package form, batch no.;

- Date and the place of occurrence of complaint;
- Cause of complaint;
- Name and address of complaint in detail.

**RESULT OF INVESTIGATIONS:** These should include:

- Result of investigation regarding market place, circulation condition and condition and condition in which the defect was observed;
- Result of investigation of retained reference sample;
- Result of investigation of analysis and testing records, production and storage records.

• Results of investigation should be referenced to the BPR of the product.

(a) Evaluation

(b) Follow up measures

Follow up measures include:

- i. Reply to the complaint,
- ii. Remedial action so those complaints of this type do not recur and or drug recall.
- iii. Competent authorities should be informed of any serious defect or problem.<sup>[1,3]</sup>

Records of complaints should be retained to evaluate trends, product-related frequencies, and severity with a view to taking additional, and if appropriate, immediate corrective action<sup>[4]</sup>. Record should be stored for an appropriate period (say ten years minimum), together with complaint samples (two years minimum)<sup>[5]</sup>.

#### **PRODUCT RECALLS: AS PER INDIAN GMP:**

Guidelines recommend that a person should be designated (authorized person) with responsibility of the execution and coordination of recall. The designated person should be provided with sufficient supporting staff. This person normally should be independent of the sales and marketing.<sup>[1]</sup>

In order to provide for all contingencies, and in accordance with Article 28 of Directive 75/319/EEC, a system should be designed to recall, if necessary, promptly and effectively products known or suspected to be defective from the market.<sup>[6]</sup>

#### **OBJECTIVE: AS PER OPPI GUIDELINES:**

##### **TO DEFINE A SYSTEM FOR:**

- a) Speedy & efficient removal of unsatisfactory material from the market.
- b) Assigning the responsibilities for implementation once the decision of recall has been made.

**RECALL APPROVING AUTHORITY:** Managing Director/ President/proprietor/Head of Company.

#### **DEFINITIONS:**

##### **AS PER OPPI GUIDELINES:**

Recall is an action taken to resolve a problem with therapeutic goods for which there are established deficiencies in quality, efficacy or safety. Two distinct types of recall are included in this Procedure:

- Permanent removal of deficient goods from the market or from use; and
- Correction, which may involve temporary removal from the market or from use.

These are designated Recall and Recall for Product Correction respectively.<sup>[7]</sup>

**AS PER TGA:** means the permanent removal of therapeutic goods from supply or use for reasons relating to deficiencies in the quality, safety or efficacy of the goods.

It includes:

- Requests to pharmacists, hospitals, pathology laboratories, fractionators, operating and research facilities, biomedical engineers or others to check and return goods found to be defective.

- Removal from supply or use of goods with inherent design or manufacturing defects.

It does not include:

- Removal of time-expired goods, and
- Removal of appropriate numbers of goods to determine whether there are deficiencies relating to quality, safety or efficacy.<sup>[8]</sup>

**CLASSIFICATION: AS PER TGA:** Recalls are classified

**Class I:** recalls occur when products are potentially life-threatening or could cause a serious risk to health.

Examples of Class I Defects

- 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
- Wrong active ingredient in a multi-component product with serious medical Consequences<sup>[8,9]</sup>

In the event of a serious or potentially life-threatening situation, local, national, and/or international authorities should be informed and their advice sought.<sup>[3]</sup>

**Class II:** recalls occur when product defects could cause illness or mistreatment, but are not Class I.

Examples of Class II Defects

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

- Microbial contamination of non-inject able, non-ophthalmic sterile product with medical consequences
- Chemical/physical contamination (significant impurities, cross contamination, particulates)
- Non-compliance with specification (e.g. assay, stability, fill/weight).
- Insecure closure with serious medical consequences (e.g cytotoxics , child resistant containers, potent products).

**Class III:** recalls 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

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

Class I or Class II recalls are considered to be urgent safety-related recalls. A safety related recall is defined under the Trade Practices Act 1974 as the recall of 'goods of a kind which will or may cause injury to any person'. Where the recall is safety-related, there is a legal requirement to notify the Minister.

Class III recalls are considered to be routine non safety-related recalls

The classification is determined by consultation between the sponsor, the Australian Recall Co-coordinator, and where appropriate, the State/Territory co-ordinator. Expert advice should be sought where the nature of the hazard or its significance is not clear.<sup>[8,9]</sup>

#### **INFORMATION REQUIRED FOR ASSEMENT OF RECALL: AS PER USFDA:**

Guidance for information to be included in the recommendation is as follows:

#### **PRODUCT DESCRIPTION (INT), TRADE NAME, AND PRODUCT USAGE FIELDS:**

- Product name and description including dosage form, strength, ARTG number,
- Pack size or type
- Batch, serial number(s), donation number(s) or tissue bank number(s).
- Manufacturer/Australian sponsor and contact telephone and facsimile numbers.
- Date manufactured and Expiry date (if relevant).
- Date released.
- Quantity of the batch, date and amount released.
- Local distribution.

- Overseas distribution of product exported from Australia.
- Number of complaints received.
- Whether the product is meant to be sterile and
- Sponsor's product/part/order code.

#### **CODE INFORMATION (RES PRODUCT DETAILS PAGE):**

Code Information (INT) field - List all lot and/or serial numbers, product numbers, packer or manufacturer numbers, sell or use by dates, etc., which appear on the product or its labeling.<sup>[10]</sup>

#### **REASON FOR RECALL RECOMMENDATION:**

Complete Reason for Recall field - provide detailed information as to how the product is defective and violates the FD&C Act or related statutes.

- Include any analytical findings in qualitative and/or quantitative terms.
- Provide inspectional (GMP) or other evidence where appropriate.
- In cases where a veterinary drug product is being recalled due to subpotency of active ingredients prior to labeled expiration date, provide the following information:
  - The firm's stability testing plan (including analytical methodology) which established the labeled expiration date.
  - Specific batch numbers in the stability studies and assay values that are the basis of the firm's recall.
  - Potency specifications which the firm uses for recall purposes.

Final assay values for the active ingredients which were the basis of the initial release of the batch. Quality Control procedures used by the firm to determine the potency of the active ingredients, is available in the EIR.<sup>[10]</sup>

#### **GENERAL RECALL PROCEDURE: AS PER TGA:**

#### **RECALL LETTERS:**

Recall letters should include 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 text of the recall letter is to be sent to the Australian Recall Co-ordinator for approval before being dispatched. The letter, which may be sent by mail or facsimile ore-mail (and then also posted if sent by facsimile or e-mail), should be dispatched within 48 hours of receiving the co-ordinator's agreement. A signed copy of the recall letter (or facsimile) to customers is to be sent to the Australian Recall Co-ordinator at this time.

- If **Class III:** 'Medicine Recall' or 'Medical Device Recall' or 'Human Blood and Tissues Recall' or 'Recall for Product Correction' or 'Hazard Alert'
- If **Class I or II:** 'Urgent Medicine Recall', or 'Urgent Medical Device Recall' or 'Urgent Human, Blood and Tissues Recall' or 'Urgent Recall for Product Correction' or 'Hazard Alert'

**Performa by Therapeutic Goods Administration Laboratories.**

1. Date of Problem: \_\_\_\_/\_\_\_\_/\_\_\_\_

2. Complainant (i.e. patient, customer, client etc.):  
Name: \_\_\_\_\_  
Address: \_\_\_\_\_  
Telephone: \_\_\_\_\_ Facsimile: \_\_\_\_\_

3. Reporter (person reporting the problem):  
Name: \_\_\_\_\_  
Occupation/Position: \_\_\_\_\_  
Institution: \_\_\_\_\_  
Address: \_\_\_\_\_  
Telephone: \_\_\_\_\_ Facsimile: \_\_\_\_\_

4. Do you consent to the release of your name and address should the sponsor or manufacturer request these details during the investigation of this problem report?  
Complainant: Yes/ No Reporter: Yes/No

5. Trade name of product: \_\_\_\_\_

6. The AUST R number (or AUST L number) of the product: \_\_\_\_\_

7. Generic name of product and strength: \_\_\_\_\_

8. Dosage form: \_\_\_\_\_

9. Pack size: \_\_\_\_\_

10. Is the pack the manufacturer's original? Yes/No (If Yes, please include)  
Batch number: \_\_\_\_\_ Expiry date: \_\_\_\_\_

12. Name of manufacturer: \_\_\_\_\_  
Address: \_\_\_\_\_

13. Name of sponsor: \_\_\_\_\_  
Address: \_\_\_\_\_

14. Full description of problem: \_\_\_\_\_

15. Date: of purchase \_\_\_\_/\_\_\_\_/\_\_\_\_ of receipt \_\_\_\_/\_\_\_\_/\_\_\_\_ of dispensing \_\_\_\_/\_\_\_\_/\_\_\_\_

16. Do you have other stock of the same batch available for testing? Yes/No

17. Has the manufacturer or sponsor been contacted? Yes/No Which?: \_\_\_\_\_

18. How were the goods stored: \_\_\_\_\_

19. Any other details: \_\_\_\_\_

Signature: \_\_\_\_\_ Date: \_\_\_\_/\_\_\_\_/\_\_\_\_ [8]

**RECALL CHECKLIST: AS PER CPSC:**

The Office of Compliance at the U.S. **Consumer Product Safety Commission** has prepared the following: recall checklist to help manufacturers, importers, distributors and retailers conduct an effective and comprehensive product safety recall. This list is a guide only to assist recalling firms in removing products from all stages of the distribution process.

**PRODUCTION:**

- Direct mail (all language must be worked out with CPSC Compliance staff)
- Toll Free Number

- Video News Release (VNR) – language follows agreed upon press release language
- Paid Advertising
- Pediatrician or Specialty Posters
- Recall (in-store) Posters
- Web-site
- a) guidelines located at cpsc web site [www.cpsc.gov](http://www.cpsc.gov)
- b) include reference to recall in prominent location on home page/first entry point
- c) link to joint press release
- d) include interactive registration of recalled product for remedy
- e) CPSC must review and approve text

• **Other Notice Forms**

- a) include recall information in product inserts
- b) include recall notice in accessory parts
- c) include recall notice in bills sent to distribution chain/consumers
- d) send direct mail notice to customers whose names are known to firm through customer service inquiries, parts orders, warranty card/product registration with company and catalogs.<sup>[11]</sup>

**EVALUATION: AS PER USFDA:**

**RECALL EFFECTIVENESS:**

It is the recalling firm's responsibility to determine whether its recall is progressing satisfactorily. The firm has an obligation to conduct effectiveness checks as part of its recall strategy. Effectiveness checks assist in the verification that all known, affected consignees have received notification about a recall and have taken appropriate action.

In some instances, a recalling firm may be unable to check the effectiveness of its recall. This could occur when a recall extends to the consumer-user level, the confidential business records of a firm's customers are not accessible, wholesalers, distributors, or retailers do not cooperate, or, because the urgency of the situation requires an all-out effort. In such cases, FDA will directly assist in this activity and, where necessary, seek assistance from cooperating state and local agencies.

Furthermore, the FDA recognizes that effectiveness checks also serve an audit function, and the agency reaffirms its policy of closely monitoring recalls and assessing the adequacy of a firm's recall efforts. Therefore, as part of its audit responsibilities, FDA will selectively conduct audit checks separately from the effectiveness checks of the recalling firm.<sup>[10]</sup>

**RECALL TERMINATION:**

FDA will terminate a recall when the monitoring district office determines that the recalling firm has completed all recall activity, including monitoring and final product disposition. The district should advise the recalling firms that FDA will not terminate a recall until the firm has brought the product into compliance or disposed of it in an acceptable manner. The district will notify the recalling firm by letter that FDA considers the recall terminated.

Termination of a Class I recall and a Safety Alert requires center concurrence. When the monitoring district concludes that such a recall or Safety Alert has been completed, the district recall coordinator will enter the information required for termination in RES on the "Summary and Termination" page. Center approval is not required for Class II or III recall terminations.

As a rule, FDA should terminate the recall within three months after the firm completes the recall. If the district feels that the recalling firm is unable to ensure that violative goods will not reenter channels of distribution, the district should consult with the CRU and/or OE/DCMO for the best course of action.<sup>[10]</sup>

**HEALTH HAZARD EVALUATION:**

**NOTE:** The following Health Hazard Evaluation Worksheet has been developed by the Agency. This worksheet, or an equivalent form, is to be used by all Center Health Hazard Committee personnel to record HHEs.

- (i) Product/identification number/usage (e.g. unit, lot, serial number, catalogue number, order number, etc.)
- (ii) Firm name, address, identification number(s). \_\_\_\_\_
- (iii) Nature of problem : \_\_\_\_\_
- (iv) (I) Have any adverse reaction reports or other indication of injuries or diseases been reported relating to this problem?  
[ ] No, [ ] Yes - attach copies or explain
- (II) Have any adverse reaction reports or other indication of injuries or diseases been reported for similar situations?  
[ ] No, [ ] yes - attach copies or explain
- (III) Is the problem easily identified by the user?  
[ ] No, [ ] yes
- (v) What segment(s) of the population is most at risk and why?  
e.g. Entire population(animals/species), infants, children, elderly, pregnant women, women of child bearing age, nursing mothers, surgical patients, immune suppressed, clinical situations, food producing animals, non-food producing
- (vi) Within the population at risk, could individuals suffering from any particular conditions or diseases be more or less at risk and if so, why?  
[E.g. immune system debilities, diabetes, cardiac problem, concomitant medications, etc.]

(vii). What is the hazard associated with use of the product? Explain and cite literature references when applicable.

- a) Life-threatening (death has or could occur)
- b) Results in permanent impairment of a body function or permanent damage to a body structure
- c) Necessitates medical or surgical intervention to preclude or reverse permanent damage to a body structure or permanent impairment of a body function
- d) No adverse health consequences
- e) Hazard cannot be assessed with the data currently available

What is the probability of an adverse event occurring?

Every time \_\_\_\_ Reasonable probability \_\_\_\_ Remote , Unlikely \_\_\_\_ Unknown

Explanation: \_\_\_\_\_

Signature: \_\_\_\_\_ Date: \_\_\_\_\_<sup>[10]</sup>

1. **GMP:** Good Manufacturing Practice, **ICH:** International Conference on Harmonization, **TGA:** Therapeutic Goods Administration, **OPPI:** Organization of Pharmaceutical Procedure of India, **FDA:** Food and Drug Administration.

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