Name of Faculty: Dr. Akhlesh Singhai

Designation: Principal & Professor

Department: LNCP, Bhopal

Subject: Quality Assurance (BP-606T)

Unit: IV

Topic: *Complaints*

COMPLAINT HANDLING IN PHARMACEUTICAL COMPANIES & PRODUCT RECALL

Dr. A.K. Singhai (Principal)
L.N.C.P ,Bhoapl

***DEFINITION*: A '*Complaint*' simply designates, that something is wrong or not good enough. Generally in the pharmaceutical industry, complaints are regarding the quality of drug product. A complaint shows customer dissatisfaction about a product and consequently, about a company.**

Principle:

- All complaints and other information concerning potentially *defective products* should be carefully reviewed according to written procedures and the corrective action should be taken.

NEED FOR COMPLAINT HANDLING SYSTEM

- ✓ It gives the company an opportunity to improve the quality of the product.
- ✓ It is helpful to maintain cGMP .
- ✓ It maintains committed relationship between the customer and company
- ✓ It is the regulatory obligation.

OBJECTIVE-

To immediately recall, investigate or to take remedial measures against the defective product.

RESPONSIBILITY-

The quality assurance manager along with manager of the complaint related department.

TYPES OF COMPLAINTS

Basically it's of three types: -

1) **Quality complaints**: Originate at consumer level and concern with physical, chemical and biological properties or condition of labeling and /or packaging of the product.
2) **Adverse reaction complaints**: Due to allergic reactions of any other untoward reaction or fatal reaction or near fatal reaction.
3) **Other medically related complaints**: Include complaints such as lack of efficacy or clinical response.

- Time period for investigation after receipt of complaints:

1. Product quality complaints – within 10 days.
2. Adverse reaction complaints– within 5 days.
3. Medical complaint – within 3 days.

✓ Complaint records shall be maintained at least one year after expiration date of medicines. Complaint records shall be reviewed and a monthly summary shall be prepared for the management

- Also the complaints are categorised as following
  - ✓Critical defects
  - ✓Major defects
  - ✓Other defects

Major Defects

- Those defects which may put the patient at some risk but are not life-threatening and will require the batch recall or product withdrawal within a few days

❑ Examples

- Any labelling/leaflet misinformation (or lack of information) which represents a significant hazard to the patient
- Microbial contamination of non-sterile products with some risk for patients
- Non-compliance to specifications (e.g. active ingredient assay)

Other Defects

- Those defects which present only a minor risk to the patient — batch recall or product withdrawal would normally be initiated within a few days

❑ Examples

- Readily visible isolated packaging/closure faults
- Contamination which may cause spoilage or dirt and where there is minimal risk to the patient

KEY POINTS FOR HANDLING COMPLAINTS

- Don't take it personally
- Never act on a complaint without hearing (at least) two sides to the story
- Say what you will do and do what you say; set the time frame
- Keep notes

DEFECTS

real

fake

25-09-2015

CONTENTS OF A PRODUCT COMPLAINT DATA SHEET

- Serial number assigned to the complaints
- Exact nature of the complaints
- Name of the complainants
- Address of the complainants
- Date of complaint received
- Name of the product, strength & batch number of the product
- Quantity involved in the complaint
- Size of the sample obtained from the complainant
- Evaluation of compliant by Q.C department
- Name and signature of the investigator & date
- Action taken by the company
- Copy of reply sent to complainant

STEPS INVOLVED IN HANDLING OF COMPLAINTS

Step 1: Receiving Complaints

It is important to have open channels with customers in order to receive their suggestions, doubts and complaints. Generally, these channels are toll-free numbers, e-mails, chat-rooms and P.O. boxes. Whatever the channel, it is necessary to have a person in charge of receiving the complaints and inputting them into an appropriate investigation form that shall be addressed to the Quality Assurance (QA) unit for investigation.

Step 2: Technical Investigation

Upon receipt of the investigation form, the QA unit is able to start the investigation, which can be divided in two phases: documentation-based and laboratory analysis.

- ***Documentation-based investigation*** - Consists of checking if this complaint occurred previously in the same lot or if any nonconformance was found in the lot during its production that could explain the complaint. The primary documentation to be reviewed in this step consists of the complaint files and the batch records.

- ***Laboratory analysis phase*** - Consists of requesting the Quality Control (QC) laboratory to analyze both complaint samples and retained samples – the reserve samples representative of the lot manufactured.

  If the customer did not send the complaint sample for analysis, the laboratory investigation will be carried out only with retained samples. Similar to the receiving step, it is fundamental that the company elects a person in the QA unit to be in charge of technical investigation of each complaint, e.g. a Complaint Officer.

After receiving the analytical results, there are three possible conclusions, as follows:

- ***Confirmed complaint*** - When both complaint and retained samples showed out-of-specification (OOS) results or when only the complaint sample showed OOS results, it is clearly a single unexplained failing product.
- ***Non-confirmed complaint*** - When both complaint and retained samples showed results in compliance with specifications or when only the complaint sample showed OOS results that cannot be considered a single unexplained failing product. OOS results in a complaint sample can be attributed to misuse or mishandling.

- ***Counterfeit / tamper suspicion*** - When the retained sample is within the specification but the complaint sample is clearly OOS with no reason for that, such as a counterfeit or tampered drug product.

Step 3: Corrective Actions and Preventive Actions

Corrective Action: eliminate detected non-conformity.

It aims to correct an existing non-conformity and to avoid reoccurrence of the same non-conformity.

Examples: arises from manufacturing deviations, OOS investigations, complaints, audit findings, recalls.

Preventive Action: prevent nonconformity occurrence.

It aims to avoid the initial occurrence of a non-conformity by proactively implementing improvements.

Examples: results from trending of in process data, of analytical data, of audit findings, trending of root causes for non-conformities or complaints, from product quality reviews (annual product reviews), quality risk analysis.

- ✓ For all confirmed complaints, corrective actions must be implemented. These actions can range from a simple and quick training to some employees to a formal Corrective Action and Preventive Action (CAPA) handling. The criteria for choosing appropriate action depends on the nature of the complaint, and the complaint incidence. If a CAPA is opened, a multidisciplinary team consisting of representatives of QA, QC, Regulatory Affairs and Production Management must be established.
- ✓ Concerning non-confirmed complaints originating from misuse or inadequate handling of the drug product, even if there is no need for internal corrective actions, corrective measures should be implemented to provide orientation to the customer.
- ✓ Regarding counterfeit or tampered suspicious complaints, a response letter should also be sent to the customer, but the Legal Affairs unit must be copied for further arrangements.

Step 4: Feed back to customers

As feedback to the customer, the company must write a response letter to the complainant to explain the investigation approach taken, the results obtained and any implications, in case the quality problem was confirmed. The customer should be sent a free replacement product together with the response letter, since the customer returned the product (the 'complaint sample') to the company for analysis and a quality problem was found.

Step 5: Monthly Reports and Trend Analysis

Monthly reports should be elaborated in order to evaluate the amount and the nature of the complaints received and to perform a trend analysis of these complaints.

RECORDING OF COMPLAINTS

It is the responsibility of the in-charge, Quality control to see that each complaint is recorded, evaluated and reported to the management. Records of complaints should include the following information:-

1. Contents of complaints - 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.

2. Results of investigation - These should include: -

- Regarding market place, circulation condition and condition in which the defect was observed
- Results of investigation of analysis and testing records, production and storage records

3. Evaluation

4. Follow up measures - It includes:-

- Reply to the complainant
- Remedial action so that complaint of this type should not reoccur.

DOCUMENTATION OF FINAL PRODUCT COMPLAINT REPORT

- Nature of the complaint _____
- Date _____
- Complaint _____
- Originator of the complaint & title _____
- Distribution contact person & title _____
- Method of notification _____
- Name _____
- Phone No. _____ P.O# _____
- Date shipped _____ Invoice# _____
- Product name _____ Control No. _____
- Expiry date _____ Quantity involved _____
- Total quantity shipped _____
- Reason for complaint return request _____
- Complaint# _____ Product _____
- Evaluation of complaints
  1. Physical characteristics _____
  2. Sign of deterioration _____
  3. Other observation _____

- Quality control findings
  1. Returned sample _____
  2. Returned sample re-assay _____
  3. Initial data _____
  4. Quality control comments & suggestions

     _____

     _____
- Quality control _____ Date _____
- Complaint# _____
- Product _____
- Packaging/Labeling/Inserts
  Evaluation_____

  _____

  _____
- Remarks _____

  _____

- Resultant action taken
  1. Method, Date of customer notification & authorized action _____

     _____

     _____

     _____

  2. Comments _____

     _____

     _____

  3. Completion date for action taken _____

  4. Quality assurance evaluation

     _____

     _____

     _____

CUSTOMER COMPLAINT REORD BOOK

Report No.	Date received	Product name	Received by	Product lot No.	Date investigation started	Date investigation ended

PRODUCT RECALL

ANNOUNCEMENT FOR DRUG RECALL

Attention: Doctors, Pharmacists, Hospitals, Distributors and Chemists

Saffron Pharmaceuticals (Pvt) Ltd., announce the immediate recall of the following drug manufactured by Saffron itself.

Product Name	Composition	Batch#	Mfg.Date	Exp. Date
Soflac-M Tablet	Diclofenac sodium & Misoprostol	01	06-2011	05-2013
Soflac-M Tablet	Diclofenac sodium & Misoprostol	02	09-2011	08-2013
Soflac-M Tablet	Diclofenac sodium & Misoprostol	03	10-2011	09-2013
Soflac-M Tablet	Diclofenac sodium & Misoprostol	04	10-2011	09-2013

The recall has been necessitated due to problem in stability. All chemists, wholesalers, hospitals and institution are advised to return any stock of the above referred batches in their possession. The stock may be returns to our distribution or directly to our head office in Faisalabad immediately and in any case not later than August 20, 2012 within one month of the announcement and obtain refund. Return of left over stock is the responsibility of chemists, wholesalers, hospitals and institutions and Saffron Pharmaceuticals (Pvt) Ltd., shall not be responsible for replacement and reimbursement of any stock of the above batches not returned latest by August 20, 2012.

Manager Quality Assurance
Saffron Pharmaceuticals (Pvt) Ltd., 19-Km, Sheikhupura Road, Faisalabad
Tel:+92-41-4364214-18 Fax:+92-41-4364219

PRODUCT RECALL

- *DEFINITION*: A process for withdrawing or removing a pharmaceutical product from the pharmaceutical distribution chain because of defects in the product, complaints of serious adverse reactions to the product and/ or concerns that the product is or may be counterfeit. The recall might be initiated by the manufacturer, wholesale dealer licence holder, or Department of Health.
- *PRINCIPLE:* "There should be a system to recall from the market promptly and effectively, products known or suspected to be defective."

Reasons for Recall

- Customer complaint
- Detection of GMP failure after release
- Result from the ongoing stability testing
- Request by the national authorities
- Result of an inspection
- Known counterfeiting or tampering
- Adverse reaction reporting

OBJECTIVES:

- To stop the distribution and sale of the affected product.
- Effectively notify Management, customers and regulatory authority.
- Efficiently remove the affected product from the marketplace, warehouse and/or distribution areas.
- Dispose and Conduct a root cause analysis and report the effectiveness and outcome of the recall.
- Implement a corrective action plan to prevent another recall.

RESPONSIBILITY:

- General manager / vice president: QA/QC Regulatory
- General Manager: manufacturing.
- Regulatory GM Manufacturing GM, Formulation and Development Medical advisor Vice president - Marketing Vice president – International Marketing Vice president – Technical Operations

RECALL CLASSIFICATION

FDA classified the product recall depending on the health hazard caused by the product in the following way:

Class I Recall- A situation in which there is a reasonable probability that the use of, or exposure to, a violative product will cause serious adverse health consequences or death. EX: Correct product but wrong strength, Microbial contamination of sterile injection or ophthalmic product , Wrong active ingredient in a multi-component product with serious medical consequences

Class II Recall- A situation in which use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences EX: Mislabeling, wrong or missing text or figures ,Missing or incorrect information- leaflets or insert.

Class III Recall- A situation in which use of, or exposure to, a violative product is not likely to cause adverse health consequences. EX:Faulty packaging , wrong or missing batch number or expiry date ,Faulty closure ,Contamination- microbial spoilage, dirt or detritus, particulate matter .

- RECALL STRATEGY: A planned specific course of action to be taken in conducting a specific recall, which addresses the depth of recall, need for public warnings, and extent of effectiveness checks for recall.

- DEPTH OF RECALL: Depending on the product's degree of hazard and extent of distribution, the recall strategy will specify the level in the distribution chain to which the recall is to extend, i.e., wholesaler, retailer, user/consumer.

RECALL NUMBER: Number assigned for each recalled product by a responsible centre. This number consists first of a letter designating the responsible centre (letter codes), a 3-digit sequential number indicating the number of recalls. Initiated by that centre during the fiscal year, and a 1-digit number indicating the fiscal year the recall was initiated.

For e.g., F-100-2 identifies the 100th recall initiated by the Centre for Food Safety and Applied Nutrition in FY-2002.

Letter	Centre/Office
F	Foods-CFSAN
D	Drugs-Centre for Drug Evaluation and Research (CDER)
Z	Medical Devices & Radiological Health-CDRH
V	Veterinary Medicine- Centre for Veterinary Medicine (CVM)
B	Biologics-Centre for Biologics Evaluation and Research (CBER)
N	Medical Devices (Voluntary Safety Alerts and Notifications)
A	Audit Numbers issued by the District performing the recall, the Centres, Office of Enforcement Division of Compliance Management and Operations [DCMO], or the Division of Field Investigation [DFI] to monitor recalls requiring audit checks.

RECALL TEAM

The Team is responsible for co-ordinating all aspects of the product recall. A recall coordinator, is to be appointed and members of a recall team identified from the various functional areas. Together the team will assist the Recall Coordinator in the event of the recall.

The Recall Management Team list shall be updated at least four times a year to ensure all names, contact phone numbers and responsibilities of team members

Name	Alternate person	Business phone	After hours phone	Responsibilities during recall
Chief Executive Officer	Production Manager			➢ Decision making ➢ Media communication ➢ Contacting accounts ➢ CFIA/Health departments contact ➢ Obtaining legal counsel
Q.A Manager	Production Manager			➢ Q.A/Technical advisory ➢ Complaint investigation ➢ DFIA/Health departments contact

LIST OF FORMS REQUIRED FOR RECALL

- Notification of Withdrawal
- Notification of Recall
- Recall Log
- Problem Report
- QA Incident Hold Form
- Receiving Log
- Shipping Log
- Recipe(s)

Process Flow of Statutory recall

Initiated by DDA

↓

Received by Manufacturer/Authorized Importer

↓

Communication to Distributors/Wholesalers / Retailers (as applicable)

↓

Distributor / Wholesalers calls back the distributed quantity of product / batch

↓

Receipt, labeling & storage of recalled stock

↓

Investigation of Product / Batch by QA

↓

Root Cause Identification, CAPA & Documentation

↓

Communication of Investigation findings

↓

Reconciliation & Disposition of recalled batch (if any)

↓

Closure of recall

VOLUNTERY RECALL BY MANUFACTURERS :

Identification of a potential non-compliance Issue

↓

Communication to QA

↓

QA to take decision on recall as per the SOP of the manufacturing firm

↓

Inform DDA where product is marketed

↓

Recall log-in by QA

↓

Communication to Distributor / Wholesalers

↓

Distributor / Wholesalers calls back the distributed quantity of product / batch (es)

↓

Receipt, labeling & storage of recalled stock

↓

Investigation of Product / Batch by QA

↓

Root Cause Identification, CAPA & Documentation

↓

Communication of Investigation findings

↓

Reconciliation & Disposition of recalled batch (if any) ⟶ Closure of recall

RECALL PROCEDURE

RECALL NOTIFICATION/ INSPECTION

- Potentially violative product which may lead/ has lead to a class I or class II recall, an inspection should be made to determine the root cause(s) of the problem(s). If the firm has failed to take appropriate preventive action, violations should be documented for possible regulatory action.

INSPECTION PROCEDURES

- To identify the root cause for the recall and assure the firm has implemented procedures to prevent it from reoccurring.
- Verify the steps taken were sufficient in depth and scope and reflect the correct conclusions about both the problem and correction.
- Determine if the firm conducted a failure analysis using techniques such as fault tree analysis or failure mode analyses, considering things such as the length of time the product has been manufactured and sold, complaints or returns for the same or similar problems, any reworking of product prior to release or distribution which may have been due to the same or similar problems and, process or personnel changes which occurred about the time the problem appeared.

For all recall inspections in addition to verifying the identification of the root cause:

1. Issue a notice of inspection (FDA 482)
2. Discuss the suspected problem with management and review the firm's complaint file.
3. Investigate all areas, control points and/or circumstances which may have a bearing on the product's deficiency.
4. Fully develop individual responsibility for the problem.
5. Review batch records, processing logs and/or other types of records for violative lots and associated lots.
6. Review and obtain copies of the firm's quality control/analytical data.
7. Determine any actions the firm has taken, is taking, or has planned to take to prevent similar occurrences. If corrective action is not underway, determine the firm's timetable for achieving correction.
8. Determine what action the firm has taken or plans to take, and the time frames involved, regarding questionable product(s) remaining in commerce.

RECALL DECISION FOLLOW –UP

- If the firm has decided to recall, steps to be followed:

1. Management should obtain their FDA District's review of recall correspondence and any press releases before they are issued to prevent misunderstandings between the firm, its customers and the FDA.
2. Obtain an official sample of the recalled product.
3. Obtain a complete distribution list of all shipments of the suspect lot(s), including foreign distribution.
4. Obtain specimens or copies of all labels and labeling associated with the recalled product.
5. Obtain complete copies of all recall communications issued or planned including the text of phone conversations, and submit them to District's recall coordinator.
6. Advise the firm on handling the returned products. Coordinator must witness or otherwise verify the reconditioning or destruction of the products returned under the recall.

CORRECTIVE ACTION

1. Describe the corrective action taken to correct the immediate problem, e.g., redesign, modify SOP, process validation, etc.
2. Qualify / validate the corrective action.
3. Establish the responsibility to assure that the corrective action would be implemented and satisfactorily completed?
4. Action taken to prevent recurrence of the non-conformance, e.g., training, increased process monitoring, etc.
5. Information provided to those responsible for the areas in which the non-conformance occurred.
6. To determine changes needed in procedures and to validate and implement the changes.

RECALL PROCEDURE

1. **Recall alert**: A recall situation exists or is planned; a twenty four hour alert will be given to the firm by the authority.
2. **Recommendation for recall number**: A memorandum should be prepared as soon as the recall number is available & transmitted to the District co-ordinator through the supervisor.
3. **Recall product**: For each recalled product, provide: its name; type (eg: tablet, sugar coated); strength, size, form; route of administration; shipping or unit package; & a brief description of the product. Indicate whether it is a prescription (RX) or over the counter (OTC) product. If the health hazard is dependent on use, consult the firm's catalogue, the red book or similar sources for that information.

   Also provide: the brand name, name, address, of the responsible firm the on label; complete copy of all labelling (including product inserts or information sheets) should be documented.
4. **Code:** List all lot &/or serial number, product number, manufacturer numbers, etc which appears on the product or its labelling.
5. **Recalling firm/manufacturer**: Provide complete name & address of the recalling firm & identify the type of firm i.e., manufacturer, importer, own label distributor. Provide complete name & address of the manufacturer if different from the recalling firm.

6. **Reasons for re-call recommendation**: Provide detailed information as to how the product is defective & violates the related statutes.

a. Include any analytical findings in qualitative &/or quantitative terms, from the firm.

b. Provide inspectional (e.g. GMP) or other evidence, where appropriate.

c. List in chronological order any complaints, injuries, or associated problems with the product.

Explain all state involvement in the recall, including sample collection or the analysis, recall agreement or initiation, recall monitoring and product disposition.

7. **Volume of product in commerce**: Provide total product distributed, also estimated amount & availability of stocks remaining on the market, at all levels. Include product expiration dates or shelf-life expectancy.

8. **Distribution pattern**: Report the areas of distribution, the number of direct accounts, and the approximate percentage of each type of consignee. List foreign countries & government military &/or civil units/agencies to which products were distributed.

9. **Firm's recall strategy**: Describe the firm's planned recall strategy. The firm's strategy should include the intended course of action when an account which distributed the recalled product is found out of business. Include the date the recall was initiated.
10. **Firm official**: Report the name, title, location, & telephone number of the firm official to be contacted concerning the re-call.
11. **Audit program**: Report appropriate action taken & also provide details of any publicity issued or planned by the firm, the state or local government.

    Provide proposed program for monitoring the recall, include time table for reviewing the recall status.
12. **Monitoring recalls**:

I. *Inspections to monitor recall progress*: Re-inspect the firm between the initiation & close out of recall to monitor its progress & verify the recalled product's disposition.

II. *Recall audit checks*: A recall audit check is a personnel visit, telephone call, letter, or a combination there of to a consignee of a recalling firm or a user or a consumer in the chain of distribution. It is made to verify all consignees at the recall depth specified by the strategy have received notification about the recall & have taken appropriate action.

III. *Conducting the check*: During the audit, the firm should furnish the following information to the authority:

a. Details of the recall
b. Recall strategy
c. About the notification received, understood & followed.
d. Date & method of notification.
e. Amount of product recalled on hand at time of notification.
f. Amount returned & the method of return, amount destroyed & method of destruction.
h. Date of anticipated return or destruction & planned method.
i. If injury reports or complaints been received, furnish report details.
j. Visit the storage sites for the recalled product,check the shelf stock to ensure all recalled product has been identified, removed from areas &properly quarantined.

IV. *Audit checks reporting*: If audit check discloses recalled product being held for sale, has not been initiated, document the responsibility for failure to follow recall instructions. An official sample should be collected from these remaining products & encourage the consignee to follow the recalling firm's instructions.

V. *Recall terminated/recall completed*: A recall will be terminated if efforts have been made to remove or correct the violative product in accordance with the recall strategy or has been made commensurate with the degree of hazard of the recalled product.

Written notification that a recall is terminated will be issued by the authority to the recalling firm.

VI. *Close-out inspection*: The final monitoring step is a limited inspection made to verify recall close out by the recalling firm. A memorandum should be prepared duly by the compliance officer, concerned authority.

During the closeout inspection, witness destruction or reconditioning of the recalled product is done. If unable to witness the destruction or reconditioning, a written documentation from the firm should be obtained. If hazardous items have to be disposed requires the firm to file an Environmental impact statement or pre-disposal processing to render the goods harmless.

INDIAN PHARMACEUTICALS LIMITED
STANDARD RECALL LETTER

Dear customer:

It has come to our notice (product name) _____ having batch number _____ or has shown _____ _

Please refrain from prescribing or dispensing any of this batch number and return all your stock of this batch number to our office at:

_____

_____

_____

All returned stock or this batch number will be replaced as free of charge. We apologies for any inconvenience caused to you and thank you for your co-operation.

Yours faithfully,

G.M. QA/QC Regulatory

INDIAN PHARMACEUTICALS LIMITED
MEDICINE RECALL OR WITHDRAWAL PROCEDURES

Press statement:

- Issued by:
- Date:
- Time:
- INDIAN PHARMACEUTICALS LIMITED, a pharmaceutical company wishes to advise a single batch.
- Number _____ of _____ has been _____ in patients were _____ a serious risk may exist. Patients in possession of this particular batch number are requested to refrain from using it.
- _____ _____ _____ _____ _____

INDIAN PHARMACEUTICALS LIMITED
MEDICINE RECALL OR WITHDRAWAL, PROCEDURE STATUS REPORT

- Date: _____ Product: _____ Strength: _____
- Pack size: _____ B. no: _____ Exp. Date: _____
- Nature of defect: _____
- Reason for recall: _____
- Indication of health risk or any other reason:
- _____
- _____
- Reported clinical problems:
- _____
- _____
- Method of communication to users:
- Method Action Date Target-group
  Number
- Phone
- Fax
- Letter
- T.V
- Radio
- Press

Disposal of waste.— (vii) The disposal of sewage and effluents (solid, liquid and gas) from the manufactory shall be in conformity with the requirements of Environment Pollution Control Board. (viii) All bio-medical waste shall be destroyed as per the provisions of the BioMedical Waste (Management and Handling) Rules, 1996. (ix) Additional precautions shall be taken for the storage and disposal of rejected drugs. Records shall be maintained for all disposal of waste. (x) Provisions shall be made for the proper and safe storage of waste materials awaiting disposal. Hazardous, toxic substances and flammable materials shall be stored in suitably designed and segregated enclosed areas in conformity with Central and State Legislations.