Unit - 4

Complaints :

→ Complaint is defined as the statement that is something wrong or not good enough, which shows customer dissatisfication about the company & the product.
Ex - Complaint about packaging material, concerning about the product, etc.

→ Customer could be internal or external.
- Internal customer is someone within your company who uses your product or services. like warehouse, quality control.
- External customer is an outside organization that receives a product or service from company like Hospitals, pharmacies, drug stores.

→ It can be two forms of complaints i.e. written or verbal:
- The written complaints are received in writing.
- The verbal complaints are received by oral & must be document by appointed person.

Types of Complaints -

(1) A- Type Complaints :
Critical complaints in which product is required to be withdrawn from the market. Such as :-
(1) Adverse drug Reaction.
(2) Major health hazard causing death.
(3) Purity & Safety.
(4) Potency
(5) Product Stability

(2) B-Type Complaints :
Major Complaints Such as :-
(1) Problems with primary packaging of the product.
(2) Chemical / Physical attributes of the product.
(3) Extraneous contamination, mix ups, etc.

(3) C-Type Complaints :
Minor Complaints Such as :-
(1) Problems related to labelling / coding batch details
(2) Shortages.
(3) Secondary packaging material problems, etc.

Responsibility -
(a) Production Head
(b) Quality Assurance Head.
(c) Unit Head.

Steps involved in Handling of Complaints -
Handling of Complaint is done in four basic steps :
(a) Receiving complaints
(b) Technical investigation
(i) Documentation based investigation
(ii) Laboratory analysis phase
(iii) Confirmed Complaint
(iv) Non-Conformed Complaint
(v) Counterfeit / tamper Suspicion
(c) Correction Action & feedback to customers
(d) Monthly Reports & Trend analysis.

Step-1 Receiving Complaints

Customer

↓

Company's Contact person

↓

QA Complaint officer

Step-2 Technical Investigation

↓ Start the investigation

Documentation - Based investigation | Laboratory Analysis Phase

↓

Q.A Complaint officer

Confirmed Complaints | Non-Confirmed Complaints | Counterfeit / tamper Suspicion

↓

Step-3 Corrective action & feedback to customer

↓

Corrective Action | Feedback to the Customer

↓

Step-4 Monthly Reports & Trend Analysis

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

Evaluation of complaint:

(1) A person shall be designated responsible for handling the complaints.

(2) Head of Quality Assurance / Quality control shall be involved all actions taken:
- Including investigation to find the root cause, checking of retention samples & batch related documents
- The eventual decision made shall be recorded.

(3) All investigation, root cause & action taken shall be recorded. Complaint could be on:
- Products manufactured by legitimate company.
- A counterfeit product.

(4) All decisions & measures taken as a result of a complaint shall be recorded & referenced to the corresponding batch records.

(5) For recurring problem, a trending shall be established in order to identify the possible systemic defects.

Handling of Returned Goods:

Pharmaceutical products can be returned from market for various reasons.

eg - Quality problems, accidental damage of goods.

Such products when returned from market should have the following action immediately taken on it:

(1) Physically examine the condition of the goods returned. Also check all the relevant documents.

(2) Ask Q.C department to evaluate the quality of the goods received & take a decision on whether these products can be reprocessed, recovered or need to be destroyed.
(3) If it is possible to reprocess & recover, then such products after reprocessing & retesting may be considered for relabelling, repacking & reselling the same.
(4) Q.C. department should evaluate all aspects of the received material.
(5) Whenever even a slightest doubt arise about the quality of the product, it should not be considered suitable for reissue or reuse.
(6) Any action taken should be recorded.

Handling of Recalling :
'Recall' means a firm's removal or correction of a marketed product that the Food & Drug Administration considers to be in violation of the laws it administers & against which the agency would initiate legal activities.
Eg - Seizures.

Objectives of recall plan -
- Stop the distribution & sale of the affected product.
- Effectively notify management, customers & regulatory authority.
- Efficiently remove the affected product from the market place, warehouse or distribution area.
- Dispose & conduct a root cause analysis & report the effectiveness & outcome of the recall.
- Implement a corrective action plan to prevent another recall.

SOP Recall Responsibilities -

- General manager / vice president : QA/QC, Regulatory
- General manager : manufacturing.

In case of adverse event a committee evaluate the crisis. It consist of following individuals :

- GM / VP/QA/QC, Regulatory.
- GM manufacturing
- GM, formulation & Development
- Medical advisor
- vice president - Marketing
- vice president - International marketing
- vice president - Technical operation.

Recall classification -

Acc. to FDA classified the product recall depending on the health hazard caused by the product :

(1) Class I Recall :

Class I is 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.

Eg - . Pathogen in ready to eat : Salmonella, E. coli.
. High levels of Sulfites.
. High level of heavy metals.

(2) Class II Recall :

Class II is a situation in which use of or exposure to a violative product may cause temporary or

medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote.

eg - Foreign objects that pose a physical hazard.

(3) Class III Recall:

Class III is a situation in which use of or exposure to a violative product is not likely to cause adverse health consequences.

Product Recall Chart -

(1) Assemble the recall management team.
(2) Notify health agencies
(3) Identify all products to be recalled.
(4) Retain & segregate all products to be recalled which are in the firms control.
(5) Prepare the press release.
(6) Prepare the distribution list.
(7) Prepare & distribute the notice of recall.
(8) Verify the effectiveness of the recall.
(9) Control the recalled products.
(10) Decide what to do with the recalled product.
(11) Fix the cause of the recall if the problem occurred at your facility.

Health Hazard Evaluation -

- An evaluation of the health hazard present by a product being recalled or considered for recall will be conducted by an ad hoc Committee of FDA.
- It involves the assessment of hazards to various segment of the population, degree of seriousness, likelihood of occurrence, consequences, etc.

Recall Team -

- A recall coordinator is to be appointed & members of a recall team identified from the various functional areas.
- All members must ensures that all procedure are carried out effectively & efficiently. The team should receive appropriate training.
- The Recall management Team list shall be updated atleast 4 times a year.

Recall Strategy -

A recall strategy that takes into account the following factors -

(a) Results of health hazard evaluation.
(b) Ease in identifying the product.
(c) Degree to which the product's deficiency is obvious to the consumer or user.
(d) Degree to which the product remains unused in the market place.
(e) Continued availability of essential products.

Termination of Recall -

A recall will be terminated when the FDA is confident that product has been removed from market in accordance with recall strategy. FDA's written notice to the regulate is the real termination.

Handling of Waste Disposal :

Pharmaceutical wastes are potentially generated through a wide variety of activities in the health care system, including syringes, & are not limited to iv preparation. Generally pharmaceutical waste may include:

- Expired drugs.
- Patient's discarded personal medications.
- waste materials containing excess drugs. (syringes, vials, etc)
- waste materials containing chemotherapy drug residues.
- Containers that hold acute hazardous waste drugs.
- Open container of drugs that cannot be used.
- Drugs that are discarded.
- Contaminated garments, absorbents & spill cleanup material

Types of pharmaceutical waste -

Types of waste	Example
(i) Communal waste	Cardboard boxes, paper, food waste
(ii) Biomedical waste	Cultures, tissue, dressing, Swabs
(iii) Anatomical waste	Recognizable body parts
(iv) Sharps	needles, scalpels, Knives, blades
(v) Pharmaceutical waste	Expired medicines
(vi) Genotoxic waste	wastes containing genotoxic drugs & chemicals
(vii) Chemical waste	Laboratory agents, film developer
(viii) Pressurized containers	Aerosol cans, gas cylinders
(ix) Radioactive waste	Unused liquids from radiotherapy

Methods of Waste Disposal:-

(i) **Incineration:** It is an effective method used for disposal of wastes, in which solid organic wastes are subjected to combustion so as to convert them into residue & gaseous products. This method is useful for disposal of residue of both solid waste management & solid residue from waste water management. This process reduces the volumes of solid waste to 20-30% of the original volume. Incineration & other high temperature waste treatment systems are sometimes described as "thermal treatment". It converts waste materials into heat, gas, steam, ash.

(ii) **Autoclaving:** In autoclaving, saturated steam in direct contact with the BMW in a pressure vessel at time lengths & temperatures sufficient to kill the pathogen are used for sterilization. Minimum temp., pressure & residence time for autoclaves for safe disinfection are specified in the Biomedical waste Rules.

(iii) **Microwaving:**
Application of an electromagnetic field over the BMW provokes the liquid in the waste to oscillate & heat up, destroying the infectious compounds by conduction. This technology is effective if the ultra-violet reaches the waste material.

Advantages - This treatment technology are its small electrical energy needs & no steam requirement.

Disadvantages - · The need for qualified technicians & frequent breakdown of shredders.
· Requires medium Investment & operating cost.

(iv) Chemical Disinfection: It is most suitable for treating liquid wastes such as blood, urine, stools or healthcare facility sewage. Addition of strong oxidants (chlorine compounds or phenol compounds) kill or inactivates pathogens in BMW. However, microbiological cultures, mutilated sharps, can also be treated by chemical disinfection.

(v) Secure land filling: Secure land filling involves disposal of solid BMW's at a landfill designed & operated to receive hazardous wastes.
The Biomedical waste Rules require disposal of discarded medicines, cytotoxic drugs, solid chemical wastes & incineration ash in secured landfills. Disposing of waste in a landfill involves burying the waste & this remains a common practices.

Document maintenance in Pharmaceutical industry:

Batch Formula Record:

Batch formula record is also known as 'Batch Processing Record' or 'Batch production & Control Record (BPCR)'

FDA defines Batch as a "specific quantity of a drug or other material intended to have uniform character & quality, within specified limits, & produced according to a single manufacturing order during the same cycle of manufacture."

A typical batch formula record in ph. industry ideally consist of these details:

(1) The products name & the size & no. of the batch.
(2) The dates of different production stages.
(3) Production details including reference to the main equipment used & yields.
(4) The batch or reference no. or analytical control no. if any of starting material used in the production.
(5) The in-process controls conducted & their results.
(6) Details of & signed authorisation of any intended deviation from the master formula.
(7) Any recovered materials & procedures applied.
(8) Initials of the operators & date & signature of the person responsible for the production.
(9) Analytical records related to the batch or reference that will permit their retrieval.
(10) A decision for the release or rejection of the batch for sale along with the date & signature of the person who will take the decision.
(11) The production record review.

Master formula Record:

Master formula Record is also known as "Master Production instruction" or "master production & control Record (MPCR)

A set of document specifying the starting material with their quantities & the packaging materials, together with a description of the procedures & precaution required to produce a specified quantity of a finished product as well as the processing instruction including the in-process control".

The master formula record should include the following details:

(1) Name & strength of the product along with dosage form. (2) MFR No.
(3) A complete list of all ingredients with their quantity.
(4) Description of containers, closures & Packaging materials to be used.
(5) Description of all vessels & equipments used in the process.
(6) Processing & Packaging instruction.
(7) IPQC's to be exercised during processing & packaging
(8) Storage condition & labelling condition of the products & their containers.
(9) Any special precaution to be observed.
(10) Packing details & specimen labels.

SOP:

- SOP is 'Standard operating Procedure'.
- SOP is defined as a set of written instructions that document a routine or repetitive activity followed by an organization."
- SOP is the backbone of pharmaceutical industries.

SOP Style Writing -

(1) SOPs shall be written in a concise, step by step, easy to read & follow format.
(2) Information should not be complicated. The active voice & present verse tense should be used.
(3) It should be simple & short.
(4) Routine Procedures that are short & require few decision can be written using simple steps format.
(5) Long Procedures consisting of more than 10 steps, with few decision should be written along with graphical format or hierarchical steps.
(6) Procedures that require many decision should be written along with flow chart.
(7) Requirements for document identification & control, accountability & traceability responsibility must be included with every SOP, this can be achieved by providing consistent format.

While writing SOP -

→ Do not Do

- Introduce acronyms without explaining what it means.
- Don't use the word 'may', 'if possible' as it implies that the user can do something under condition. Instead be positive & tell them what to do.

→ Do -

- Write the present tense. Don't write in the past, conditional, or future tense unless you have good reason to do so.
- Avoid ambiguity.
- Be concise.
- Keep the words short & get to point.
- Make sure one idea to another link in logical manner.
- Highlight exception. Use a symbol to flag that is an exception & how to handle it.
- Highlight warning. Again, when used text cautions must be used in this document. Warning must stand out, use a larger font or a warning icon.
- Reduce the word count where possible without loosing the meaning of the text.

Benefits of SOP -

- To provide people with all the safety, business, environmental & operational information necessary to perform a job properly.
- To ensure that instructions, operations are performed consistently to maintain quality control of processes & products.
- To ensure that processes continue uninterrupted & are completed in a prescribed timeframe.
- To ensure that no failures occur in manufacturing & other processes that would harm anyone in the surrounding community.
- To serve as a checklist for auditors.

- To ensure that approved procedures are followed in Compliance with Company & goreserment regulation.
- To serue as a checklist for co-workers who observe job performance to reinforce proper performance.
- To serue as an historical record of the how, why & when of steps in existing process so there is a factual basis for revising those steps when a process or equipment are changed.
- To serue as an explanation of steps in a process so they can be reviewed in accident investigation.

Quality Audits :

→ General Format of SOP -

Name of facility _____ page ----- of -----

SOP NO. _____ Title _____

Revision No. _____

Written by _____ Edited by _____

Authorization signature _____ Department ____ Date ____

Effective date _____ Replaces _____

Purpose :

why :

why is the procedure written
why is it being performed.

Scope :

when :

Indicate when this procedure needs to be performed.

where :

Indicate where this procedure applies.

Responsibility :

who :

who perform the procedure
who is responsible to see it is performed correctly

Material & equipment :

what :

what is needed to perform the test. This list should be completely specific

Quality Audits :

"A systematic & independent examination to determine whether quality activities & related results comply with planned arrangement & whether these arrangements are implemented effectively & suitable to achieve objective."

Reasons for Quality audits -

- To determine level of compliance
- To build confidence in GMP & QA system
- To build inter departmental trust, understanding & communication.
- To determine measures necessary to improve.
- To provide a stimulus for improvement.
- To recommend corrective action
- To monitor improvement.

Types of Quality Audit -

It is classified into 3 different categories :

(i) Internal Audit : It is also known as First-Party Audit or Self-Audit. It is defined as those auditing or those being audited all belong to same organization.

(ii) External Audits: It is also known as Second-Party Audit. It refers to a customer conducting an audit on a supplier or contractor.

(iii) Regulatory Audits: It is also known as Third-Party Audit. Neither customer nor supplier conducts this type of audit. A regulatory agent or independent conducts a third party audit for compliance or certification or Registration purposes.

Steps for performing Quality Audit -
- Plan & prepare.
- Arrange & announce.
- Arrive at the site of audit meet & explain purpose.
- Perform audits.
- Informal oral report of finding.
- Formal report with recommendation
- Follow up.

Quality Review & Quality Documentation:
→ It is regular periodic review & documentation of all licensed medicinal products.

Objective-
- verifying the consistency of the existing process, appropriateness of current specification for both starting materials & finished products.
- To highlight any trends.
- To identify product & process improvement.

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→ It is an effective quality control improvement tool to enhance the consistency of the process & overall quality of the product.

Objective -

- Determine the need to make changes the manufacturing process, process control, in-process tests, product specification.
- Verifies compliance with market authorization.
- Verifies consistency of manufacturing process.
- Determines the need for re-evaluation of existing processes.
- Identification the product & processes improvements.
- Identifies any adverse trends & need to take Corrective & preventive action.

Reports & Documents:

→ "Report is defined as it gives a spoken or written account of something that one has observed, heard, done or investigated."

→ "Documents is defined as a piece of written, printed or electronics matter that provides information or evidence or that serves as an official Record.

Objectives -

(1) To define the specification & procedures for all materials & manufacture & control methods.
(2) To ensure that the personnel associated with manufacturing know their work & time of doing it.
(3) To ensure the availability of data required for validation, review & statistical analysis.

Contents of Reports & Documents -

(1) Name
(2) Subject
(3) Purpose
(4) Date & time
(5) Scope
(6) Contents
(7) Background
(8) Summary
(9) Any figures & illustration
(10) Conclusion
(11) Name & signature of authorized person.

Distribution Records:

Distribution records should contain the following:

(1) Name, Strength & dosage form description of the product.
(2) Name & address of consignee.
(3) Date & Quantity Shipped.
(4) Lot or Control no. of the drug product.

Objective -

- To ensure that adequate data are available to access trade customer.
- The recording of batch no. to each other will accomplish this purpose.

Distribution records include wide range of documentation invoices, bills of lading, customer's receipts, internal warehouse storage, inventory records.