Complaints and Recalls

Now u can type with ur eyes

Dr.K.Kathiresan.,M.Pharm.,Ph.D.,M.B.A.

Associate Professor

Department of Pharmacy

Annamalai University

v r going to deal with an area of very great importance

Product complaint principle

“ **All complaints & other information concerning potentially defective products must be carefully reviewed according to written procedures”**

Do not place the patient at risk because of inadequate safety, quality or efficacy

Objectives

- **To identify the key issues in product complaint and recall handling**
- **To understand the specific requirements for organisation, procedures & resources.**
- **To understand & develop actions to resolve current issues applicable to u**

Complaints as a tool for overall quality improvement

Complaints Handling Principle

- **Handle Positively & carefully review**
- **Must be seen as important work**
- **Managed by a senior staff member**
- **Thorough investigation of the cause is essential**
- **A major source of information & learning**

The result of investigation r used to improve the situation and prevent recalls & complaints in the future

Complaints Procedure - I

- Designated responsible person
- Written procedure describing action to be taken
- Acknowledge and respond to complainant within a reasonable period
- Record written and verbal comments

Responsible Person

- **May be authorized person**
- **If not, must advise authorized person of results**
- **Sufficient support staff**
- **Access to records**

Decision from a Complaint Investigation

Complaint justified

- Actions to prevent reoccurrence
- Ongoing observation of process
- Recall product may be required

Complaint not justified

- Advise customer of findings
- Appropriate marketing response

For example, when the product has expired for a long time or the product was not kept at the storage conditions stated by the manufacturers.

Other issues

- **Regular review of trends required**
  - **Reoccurring problems**
  - **Potential recall or withdrawal**

- **Inform competent authority of serious quality problems**

Classification of Defects

- **If complaint is justified, then there has been a failure of the quality system**
- **Once defect has been identified, company should be dealing with it in an appropriate way, even recall.**
- **The definition of defects is useful.**

- **The following system has been found in some countries (but it is not a WHO guideline):**
  - **Critical defects**
  - **Major defects**
  - **Other defects**

Critical Defects

Those defects which can be life threatening and require the company to take immediate action by all reasonable means, whether in or out of business hours

Examples

- **Product labelled with incorrect name or incorrect strength**
- **Counterfeit or deliberately tampered-with product**
- **Microbiological contamination of a sterile product**

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

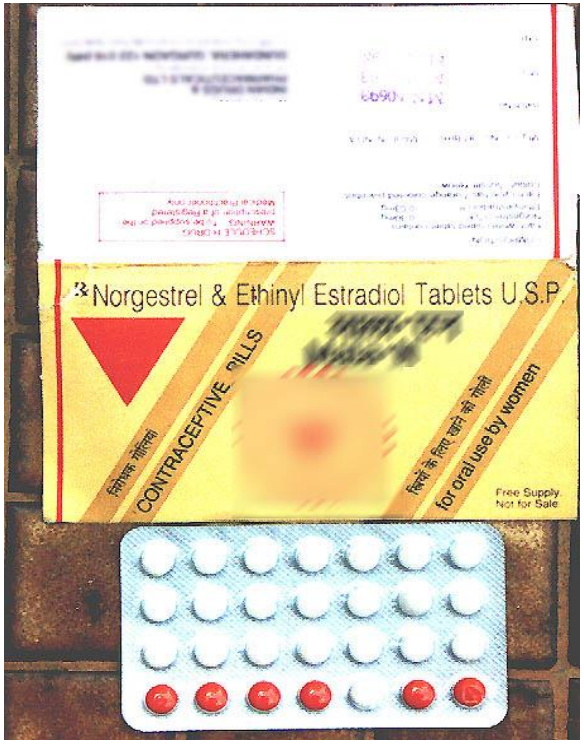
Examples

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

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

Detection of GMP failure



Product Recall Principle

“There should be a system to recall from the market promptly and effectively, products known or suspected to be defective.”

Definition

Recall

- Removal from the market of specified batches of a product
- May refer to one batch or all batches of product

Responsible person

SOP for Recall

- Established, authorized
- Actions to be taken
- Regularly checked and updated
- Capable of rapid operation to hospital and pharmacy level
- Communication concept to national authorities and internationally

Distribution Records

- Available to designated person for recall purposes
- Accurate
- Include information on:
  - Wholesalers
  - Direct customers
  - Batch numbers
  - Quantities

Collect 3 examples of complaints or recalls from your experience

Thank you

QUALITY AUDIT

Dr.K.Kathiresan,M.Pharm., Ph.D.,M.B.A.,

Associate Professor

Department of Pharmacy

Annamalai University

AUDITING IN THE PHARMACEUTICAL INDUSTRY

Medicinal products have to be of high quality

People’s lives depend on it. While end product testing of samples from each batch (to ensure compliance with a release specification) is important, it is not enough to ensure quality, which must be built into the manufacturing processes.

To ensure quality, all pharmaceutical manufactures are required to establish and implement an effective pharmaceutical QA system, involving the active participation of the management and personnel of different services involved.

To assess the effectiveness of this QA system and ensure that it follows good manufacturing practice (GMP), regular audits must be performed. Audits may be performed by the manufacturer on itself (internal), or on its vendors (external). Alternatively, audits may be conducted on a manufacturer by its customers or by a regulatory body (regulatory).

INTERNAL AUDITS

Internal audits are carried out by an organization on its own systems, procedures and facilities. European legislation requires the Pharmaceutical manufactures: ‘conduct repeated self-inspections as part of the QA system, to monitor the implementation and respect of good manufacturing practice and to propose any necessary corrective measures. Records of such self-inspections and any subsequent corrective action shall be maintained’.

Aside from the legal requirement, internal audits are vital from a business perspective. As well as monitoring the current compliance status, well-conducted internal audits help to spread the message that quality is everybody’s responsibility and to catalyse continuous improvement.

The Organisation of internal audits depends on the size and complexity of the organization. A procedure and programme of internal audits should be available and may be requested during regulatory audits. Responsibility for the management of internal audits should be assigned to ensure that they occur and are effectively followed up (always a challenge). One possible system is a three tier approach.

Tier one - audits carried out by the staff of a section or department on themselves. Such audits will typically be short and limited in scope, focusing on ‘visibles’, such as housekeeping and documentation.

Tier two - audits typically led by a local QA group, comprising staff independent of the department under audit. Such audits will typically be longer, but less frequent and are likely to focus more on systems than housekeeping.

Tier three - audits carried out by a corporate compliance group. Alternatively, external consultants may be used. Such audits are often carried out to assess readiness for a regulatory audit, but may also be used to obtain an expert view on a specific critical activity.

For tier one audits, are usually selected on the basis of knowledge and experience of the area to be audited, though they should also receive some basic training on the reasons for audits and particular areas for examination. More extensive audit training will be required for tier two auditors, with more detail on quality systems and audit techniques. Tier three auditors are likely to be highly trained and experienced specialists, with an expert knowledge of GMP and other regulatory requirements for pharmaceuticals.

EXTERNAL AUDITS

External audits are audits carried out by a company on its vendors or subcontractors. There is no legal requirement to conduct such audits, but the need is implicit, since manufacturers are required to have a thorough knowledge of their suppliers. Furthermore, if work is contracted out, they must ensure that contractors are complement to complete it, in accordance with GMP.

There are also strong business benefits to be derived from performing these audits:

- Building knowledge and confidence in the partnership arrangement.
- Ensuring that requirements are understood and met.
- Enabling reduction of certain activities (e.g. in-house qc testing of starting materials).
- Reducing the risk of failure (and, by implication, its costs).

The scope of these audits will vary, depending on the relationship between the two parties, which may range from a simple vendor-purchaser transaction to a strategic joint venture partnership. Confidentiality and technical agreements are likely to influence this.

Typically, there will be an initial evaluation audit of the capabilities and general suitability of the vendor / contractor. Subsequently, regular audits will be carried out to assess compliance with agreed contractual standards, the frequency of which will depend on the initial findings and the critically of the vendor and materials supplied. As confidence in the vendor increases through auditing, confidence in the vendor's own internal auditing systems, third-party audits and vendor history – it should be possible to reduce the level of external auditing.

External auditors typically have a broad practical experience of GMP and receive quality systems auditing training equivalent to that of ISO 9001 lead auditors. Audit teams may also include specific technical experts. Depending on the size of the facility and the scope of the audit, an audit team of one or two other people will usually accompany the audit leader.

Many Pharmaceutical industry suppliers are ISO 9001 or ISO 9002 – certified and are regularly audited by their certification body. IQA's Pharmaceutical Quality Group has published codes of practice for Pharmaceutical suppliers, under the banner 'PS 9000', detailed the additional requirements for the Pharmaceutical industry, concerning the manufacture of product contact packaging materials, printed materials and raw materials (active ingredients and excipients). Pharmaceutical contract manufacturing or packaging companies will need to be licensed and will be subject to regulatory audits.

Regulatory Audits

These audits are carried out by regulatory bodies against relevant regulations for the manufacture and supply of Pharmaceutical products. National regulatory bodies, such as the Medicines Control Agency (MCA) in the UK and Food and Drug Administration (FDA) in the USA, are statutorily responsible for carrying out such audits. All licensed Pharmaceutical manufactures periodically receive them (as may their contractors). These audits may be unannounced (MCA currently performs about ten percent of its UK inspections like this) as manufacturers are expected to be complying with GMP at all times. Regulatory bodies from other countries in which products are sold may also audit companies (i.e. FDA audits European manufactures).

Regulatory inspectors are extensively trained and are knowledgeable and professional. All MCA medicines inspectors are relevantly qualified and have a minimum of five years appropriate experience in a manufacturing operation. They will be on the registers of persons eligible to act as qualified persons (QP) and lead auditors.

Failure to pass a regulatory audit can lead practical experience of GMP and receive to restrictions on (or the withdrawal of) a manufacturing or import / export license. (FDA has recently imposed punitive financial ‘consent decrees’ on companies which failed to respond adequately to audit findings and comply with GMP). Therefore, it is vital that companies have defined processes for handling audits and that staff are well trained as auditors. Internal audits can provide valuable practice opportunities.

Currently, different regulatory bodies have distinct audit styles and requirements, but to reduce costs and the audit burden on manufacturers, there have been moves towards sharing and mutually recognizing audit findings between these bodies, a practice likely to increase in the future.

There has been a Pharmaceutical Inspection Convention (PIC) since 1971. Based in Geneva, PIC is open to any member of the UN that satisfies PIC officials of its adequate legislation and inspections relating to medicinal products. Under PIC, the health opportunities of member countries agree that, if the manufacturer consents, information obtained during inspections may be exchanged. PIC holds regular meetings for the representatives of member countries to discuss common standards.

Launched in November 1995, the Pharmaceutical inspection co-operation scheme is an informal, flexible arrangement between the inspectorates of PIC contracting states, which is run in parallel with PIC and is open to inspectorates from other countries.

The scheme retains and improves on the convention's main features:

- Networking and confidence –building between national inspection authorities
- Development of quality systems
- Training of inspectors and related experts
- Work towards global harmonization of GMP

Regulatory audits vary considerably in scope, frequently and duration. Audits by the national regulatory body are likely to be regular and to cover systematically all areas of a facility, over a period. There may be additional audits (or Visits) as a result of specific events, which may be company – specific (for example the recall of a product) or industry – wide (a recent example being checks on compliance with transmissible spongiform encephalopathies regulations by the MCA).

Audits by the regulatory body of another country may be general, or linked to a specific regulatory event: the Pre-approval inspections of the FDA are linked to submission of a new drug application. Depending on the scope, up to three, inspectors may visit, for a period of between half a day to two weeks.

After a regulatory audit, a formal report will be delivered , the format of which will depend on the regulatory body concerned. MCA provides verbal feedback at the exit meeting, then a brief, action-oriented, written report shortly afterwards, FDA provides a ‘form 483’ at the exit meeting, if there are points of concern, followed by a more detailed establishment inspection report. The regulatory body will expect a timely, formal response to the audit report and typically, will check that corrective action has taken place, as part of the next audit, it is wise business practice to take regulatory audit findings seriously and ensure that timely and effective corrective action is taken.

Thank You