How to Manage Recalls and Withdrawals of Pharmaceuticals

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WHY RECALLS AND WITHDRAWALS

CALL OF THE DAY
WHEN SAFETY AND EFFICACY OF PHARMACEUTICAL FINISHED PRODUCT THREATENS HUMAN LIFE
RECALL is defined as:

- “the returning of all or some units of a particular batch or several batches of a pharmaceutical product which has been marketed, back to the manufacturer’s warehouse so as to prevent the use of the product if a serious quality defect is either suspected or is recorded and confirmed with a possible risk to a consumer.

Differentiation between Recall and Withdrawal:

- **Recall**: recall may involve a single batch, part of a batch or several batches for reasons of quality,

- **Withdrawal**: withdrawal concerns the entire production of a product, for regulatory or pharmacovigilance reasons.
CONDITIONS OF RECALL

- Become necessary if serious quality defects are reported by:
  - External Sources (Regional distributors, Institutional distributors, Retailers, Consumers, Doctors, Hospitals and State Health Authorities).
  - Internal Sources (Sales Department, Quality Control Department, Finished Goods Warehouse, Regulatory Affairs Department).
- The defects in the quality should be classified according to following classification.
Class – I – Potentially Dangerous:

- This is a situation in which there is a reasonable probability that the use of, or exposure to, the product will cause serious adverse health consequences or death.

For Example:

- Wrong product (label and contents are different)
- Right product but wrong dosage with serious potential medical consequences
- Chemical contamination entailing serious potential medical consequences (significant impurities, cross contamination, particulate contamination, suspicion of contamination or sabotage by a 3rd party)
- Wrong active substance in a multi-ingredient product entailing serious potential medical consequences
- Third party tempering or adulteration
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- Class – I I – Defect likely to result in disease or inappropriate therapy, excluding class I
- This is a situation in which the use of the product may cause temporary or medically reversible adverse consequences or where the probability of serious adverse health consequences are remote.

For Example:

- Labeling error (text or data erroneous or missing)
- Missing or incorrect information on printed text or package inserts
- Product mix up in containers
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CLASS – II

- Non-compliance with specifications (tests/content, stability, content/weight). Deviation due to degradation of the product seen by reviewing stability

Class-III-

- This is a situation in which the use of the product is unlikely to cause adverse health consequences but for which a batch recall has been instituted for other reasons, and not covered in class I and II and excluding class I & II defects.
CLASS – III

For Example:

- Defective packaging (batch number or expiry date erroneous or missing), storage incident
- Defective closures
- Contaminated by dust or particles
- If recall becomes necessary, it must be executed immediately and efficiently. The purpose is to prevent the possibility of risk to patients or damage to the company’s public image
PRODUCT RECALL COMMITTEE:

- In order to execute the prompt recall, a recall committee must already exist. The committee will comprise of the following members:
- Chief Executive of the company.
- National Sales Manager.
- Technical Director/Head of Production.
- QA/QC (Qualified person & Recall Coordinator).
- Regulatory Affairs Manager.
- Warehouse Manager.
- The name, designation, contact numbers (telephone #, fax #, e.mail address) of the members of product recall committee must be available.
AUTHORITY TO ORDER A RECALL:

- As the qualified person (QP), designated by management (responsible for batch release) is the recall coordinator.

  Once quality defect has been detected or suspected.

- Will evaluate the need to recall.
- Once a decision has been taken, the Chief Executive Officer is informed and the recall is initiated.

DEPTH OF RECALL:

- Depending on the recall classification and the products distribution.
- Recall strategy will specify the level in the distribution chain to which the recall is to be extended.
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RECALL TYPE A: The consumer level
RECALL TYPE B: All distribution levels
RECALL TYPE C: Certain distribution levels

RECALL PROCEDURES:

- If recall becomes necessary, it must be executed immediately and efficiently.
- The purpose is to prevent the possibility of risk to patients or damage to the company’s public image.
- Top priority will be given to recall work by all concerned, even if recall has to be processed after working hours or on holidays.
PREPARATORY MEASURES:

Tasks of Recall Committee:

- The recall committee must:
- Quarantine stock and/or recalled stock.
- Either holding in stock or have distributed.
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- These must be informed of the reasons and causes for recall and of the consequences thereof.

- Specify the type and level of the recall (Distributors, Institutional Distributors, Retailer, Consumer etc.)

- Inform the local health authorities for a decision regarding recall.

- Send the recall order to Regional Distributors, Institutional Distributors and Organizations within the distribution channel.

- This procedure must be carried out as quickly as possible-using methods of communication according to the level involved (fax, telephone, mail, media print/electronic etc.)
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- They must be given a list of standard questions and answers and pass on the information through the appropriate channels (e.g., sales team).

- Where the situation so warrants, the media are to be informed by a suitable written communication where necessary for the health authorities, health care professionals, pharmacists (private, hospitals, clinics) and the distribution channel concerned.

- All products recalled are taken into stock and handled using the currently applicable return procedure.

- Carry out regular reconciliation of the concerned product (comparison of quantities returned in relation to quantities shipped).
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The persons responsible for recall will perform the following functions:

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<th>Persons Responsible for Recall</th>
<th>Responsibilities</th>
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| Chief Executive Officer       | • Facilitate the task of Recall Coordinator (QP)  
                              | • Liaison with head office regarding Recall |
| Technical Plant Head          | • Supervision of all activities within the plant regarding Recall.  
                              | • Initiation of recall in liaison with QC Manager.  
                              | • Investigation of recall in liaison with QC Manager (if applicable)  
                              | • Facilitate the task of Recall Coordinator (QP)  
                              | • Drafting the final report of recall process in liaison with QC Manager. |
| QC/QA Head (QP)               | • Coordination with Recall Committee  
                              | • Drafting the final report of recall process in liaison with Plant Technical Head. |
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| National Sales Manager         | ● Facilitate recall process through sales team.  
                                | ● Coordination with distribution channels and sales net work for tracking and recovery of recalled product.  
                                | ● Advise the sales staff to vigilantly look and seize any left over stock in the market/retailer shops. |
| Regulatory Affairs Manager     | ● Look after all legal and regulatory affairs with authorities regarding recall. |
| Warehouse Manager              | ● Ensure all contact numbers of the distributors/institutions are available.  
                                | ● Tractability of recalled product including physician samples.  
                                | ● Clearly separate segregation of recalled goods in the warehouse.  
                                | ● Record and reconciliation of all recalled goods.  
                                | ● Feed back to the distribution channels regarding the quantity received and the quantity still pending. |
The recall committee must remain available on a 24-hour basis until the complete recall of product has been accomplished.

PRODUCT DISTRIBUTION RECORD SYSTEM:

- Product distribution records are the basis of an effective recall and should be kept in such a way that the complete and quantitative distribution of any batch could be determined rapidly.
- In order to ascertain the effectiveness of the recall procedure, it should periodically be validated.
- **End of Recall:** When the product has been recalled, the recall activity will be declared completed by the recall coordinator.
- **Fate of Recalled Stock:** Fate of the recalled stock will be decided, keeping in view the classification of defects defined in clause
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- Destruction of Recalled Products: In the case of destruction, the recalled products must be destroyed according to SOP.

  The destruction can only take place after:

  - Total reconciliation of the quantity of recalled products.
  - Authorization by Chief Executive Officer.
  - Should also involve Health Authorities.
FINAL REPORT:

- A complete report drawn up by the recall/withdrawal committee must be submitted to the local health authorities giving details of all action and reconciliation, and of all action taken to investigate, understand and correct the source of the deviation that resulted in the recall/product withdrawal.

- Interim reports must be prepared until the recall/withdrawal procedure is completed.
DOCUMENTATION:

- All documents, files, letters action plan destruction/disposal record etc., of the recalled products should be suitably stored in the office of the persons responsible for recall and should be made easily available when necessary.
- All data concerning the recalled batches and all documentation concerning the recall procedure must be centralized locally and archived locally.
- Annexures will be used as the formats for the execution of recall procedure.

RECALL TEST:

- The SOP must be tested and challenged at least once per year as per a recall drill.
In 2006, 21 people died in Panama after taking a government-made cough syrup containing diethylene glycol that had been mislabeled as glycerol, a widely used excipient. Another 38 people suffered side effects including disorientation and kidney failure.

In 1996, glycerol contaminated with diethylene glycol killed 88 people in Haiti.

While in 1990-1992 paracetamol syrup contaminated with diethylene glycol from propylene glycol led to 236 deaths in India and Bangladesh.

This illustrates the view that, in most cases, problems with excipients have occurred.

Because of a failure in GMP, GSP, GDP.
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PIC
FIASCO
INVESTIGATION

CONCLUSION

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Some Serious Question:

- Was it the first incident of its kind in the world?
- How did the world respond to such incidents?
- Why the preventable deaths not stopped through stoppage of further use or effective drug recall?
- Is there any law to deal with such cases?
- Have we learnt the lessons?
- Was the investigation fair and scientific?
- Can drug related issues including pharmaceutical care be solved by everybody except professionals educated and trained on drug related subjects?
- Can health assurance needs be met without multidisciplinary approach and sincere efforts by universally recognized triangle of health care consisting of doctors, pharmacists and nurses.
THANK YOU