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An Overview on Pharmaceutical Drug Recalls

Rohit VVSS*, Jaya Prakash Veluchuri, Sravya Adhikari, Harika Indukuri

*Department of Pharmaceutical Management and Drug Regulatory Affairs, Andhra University Collage of Pharmaceutical Sciences, Visakhapatnam, Andhra Pradesh, India
Email: Rohitvoguri5@gmail.com

Abstract Every year drug recalls occurs routinely. The product recall is resorted to if there is evidence that the use and the continued presence of a batch of a product on the market presents a risk to the health of the user or a local regulatory authority directs a recall. A company must, therefore, have a system for speedy and efficient removal of unsatisfactory material from the market. There should be a written procedure that must define-who is responsible for deciding to initiate a recall and how the product, including samples, can be traced and removed from the market. Product recall not only effects the company financially but also effects company reputation, brand integrity. Thus, taking responsibility and fast actions are the safest ways to save brand recognition and public health from product recalls. So the regulatory bodies has implemented measures to ensure that the product recalls are handled properly by alerting public and removing the product safely from the market.

Keywords Drug recall, regulatory bodies, recall strategy, quality, safety

Introduction

Recall means that a firm's removal or correction of a marketed product ,that regulatory authorities envisage to be in the violation of the law it administers and against that the agency would initiate legal proceeding, e.g. Seizure. Drug merchandise products recalled once they have a potentially harmful impact on the public because of their defective quality, safety or efficacy. The recall doesn't embody market withdraws or a stock recovery. The defective products associated with quality include Not of standard Quality, adulterated or Spurious medicine. Safety and efficacy connected recalls embody serious adverse reactions and death. This has been discovered and declared as not of ordinary quality by Government Analysts, supported incidents wherever serious adverse effects or death are reported. Assessment should be made of the seriousness of the defect, its potential for inflicting damage to the patient. Legal proceeding was taken by the agency if the orders don't seem to be followed. Hence, a good recall procedure ought to be followed by the corporate to reduce harmful effects on the public. Nowadays, product recalls are common, thus firms should follow bound methods to reduce the recollects [1-6].

Types of Recalls

If any product or the batch not meeting the defined quality standards along with safety and efficacy it has to be recalled from the market [2-3].

Recalls are two types

i) Voluntary Recall
ii) Statutory Recall

i) Voluntary recall

The voluntary recall is often triggered by any incident that affects the safety, efficacy, and quality of the batch/product in question such as

1. If the batch or batches are found to be noncompliance with the regulatory specifications during the post-marketing studies.
2. If the batch is found to be defective which it is finding out from market complaint.
3. If any unusual observation is founded during a visual inspection of retention samples which indicate an impact on the quality of the product after investigation.
4. If the pharmacovigilance reports indicate that there is a serious risk associated with the product.

ii) Statutory recall:

Statutory recalls are often triggered in response to the direction or mandate by the Drug Regulatory Authorities (Central/State) in one or more of the circumstances as follows

1. To recall the drug product/batch., if they are out of standard quality etc.
2. To recall the banned drugs.
3. Labeling and/or Promotional materials, that are considered to be in violation of the law.

Recall Classification

Recall classification is a numerical designation i.e., I, II, or III assigned by Food and Drug Administration to a particular product recall to indicate the relative degree of health hazards presented by the product being recalled [1-4].

Classification	Description	Examples
Class I	The product will cause serious adverse health consequences or death.	A label mix-up of a lifesaving drug.
Class II	Product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote.	A drug that is under-strength but is not used to treat life-threatening situations.
Class III	The product is not likely to cause adverse health consequences.	A minor container defect.

The Effective Time Period for Recall

The recall is an effective method of removing or correcting consumer's products that are in violation of laws by the Regulatory body. The manufacturer should decide the time period within which recalls being completed for that class, For example

Class I -Recall should be started immediately and it should be completed within 12 to 14 hours from the consumer level.

Class II- started within 48 hours.

Class III- started within 3 days.

Recall may be undertaken voluntarily and at any time by the manufacturer and distributors, or at the request of the Regulatory body. A recall is usually more appropriate and affords higher protection for customers than a seizure [3].

Reasons for Recall of the Product

A distributed product can be called back for various reasons. Some of the reasons can be as follows:

i) Product complaints by customers reveal that the product is sub-standard, and hence the manufacturer decides to recall the product.

ii) Regulatory body officials find that a sample drawn by them from the market and analyzed by the government analyst's lab shows the product to be sub-standard and asks the manufacturer to recall the product.

iii) Sometimes stocks at various depots, etc. are affected by natural calamities like floods, etc. and get damaged. When this information comes to the manufacturer he recalls the product or asks to return the product.

iv) The manufacturer himself may find problems with the product, such as substandard quality, which has been detected after the release of the product, problems related to the stability of the product; or based on the market complaint received from a consumer or medical practitioner.
v) Accidental damage to the consignment my also happens during transportation. In such a case the product quality is not questionable, but packages might get broken and can't be sold or distributed as such in the market, and hence needed to be recalled [2].

Recall Strategy

Depending upon the product degree of hazards and extent of distribution, the recall strategy will specify the amount of distribution to which the recall is to extend as follows:
i) Consumer or User Level: which can vary with product, together with any intermediate wholesale or retail level. Consumers or users might include individual consumers, patients, physicians, and hospitals.
ii) Retail Level: It includes retail groceries, pharmacies, hospital pharmacies, dispensing physicians, institutions such as clinics and nursing homes, etc.
iii) Wholesale Level: all distribution levels between the manufacturer and retailer [1].
The purpose of a public warning is to alert the public that a product presenting serious health hazards. The manufacturer should submit the public warning plan to the Regulatory body. The recall strategy can specify whether or not a public warning is required and whether or not it'll issue as;
i) General public warning through the general news either national or native.
ii) Public warning through specialized news media e.g. professional or trade press, or to specific segments of the population such as a physician, hospitals, etc [11].

The recall strategy will specify the strategies to be used for and also the level of effectiveness checks which will be conducted as follows

i) Level A- 100% of the total number of consignees to be contacted;
ii) Level B- Some % of the total number of consignees to be contacted, which % is to be determined on a case-by-case basis, but is greater than 10% and less than 100% of the total number of consignees;
iii) Level C- 10% of the total number of consignees to be contacted;
iv) Level D- 2% of three total number of consignees to be contacted;
v) Level E- No effectiveness checks [2-4]

Pre-Recall Investigation

Any product complains from consumer or field staff should be promptly referred to the quality control department for investigation and recommendation for recall, if so required. Any batches of the product found unsatisfactory and necessitating recall shall be evaluated for the level of recall (i.e. intra-company, wholesale, retail, etc.,) and approving authority shall within in a period of 2 days, approve the recall. In case of receipt of a notice from Drug Control authorities, any in-house investigation should be completed within 2 working days unless exigencies justify longer investigation time. Upon approval of recall, a recall coordination committee consisting of the head of quality control, sales, and marketing, distribution, warehouse, and production, shall designate one person to exclusively coordinate all communications, on behalf of the company, with the distribution outlets and the drug control authorities and with the committee and its members. Therefore by monitoring the recall, an investigation report is prepared [11-12].

Recall Process

A) The recall process follows three approximate phases. Distinct difficulties arise based on the kind of drug being recalled.

Drug recalls can be initiated by the producing firm or the Regulatory body, and those launched by the regulatory body can be either mandatory or voluntary. This applies not just to drugs but all products covered under the regulatory body (fig-1).

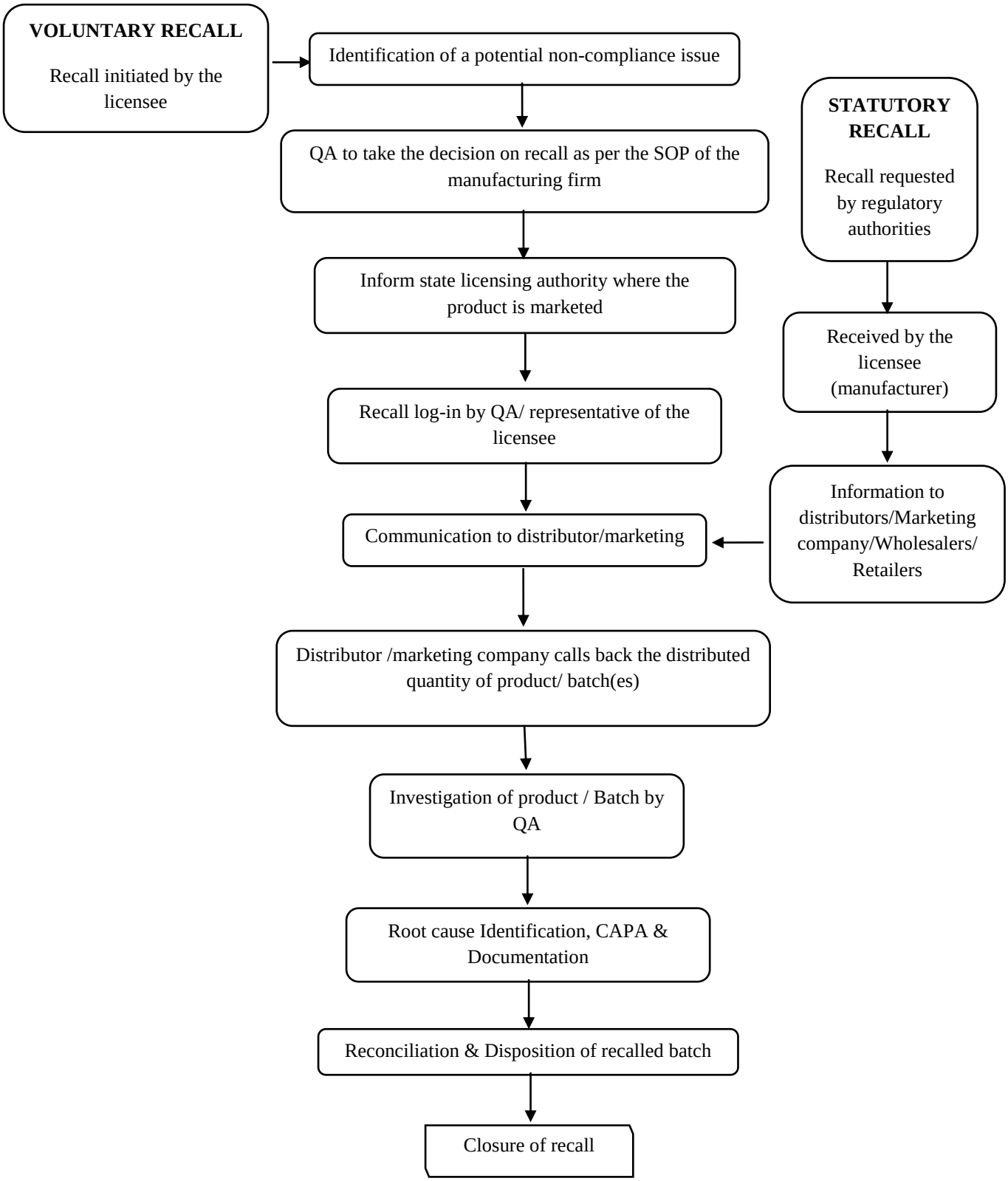

Figure 1: Recall Procedure [3]

1. Notification and response

A firm submitting a recall to the Regulatory body must provide all relevant information about the specific drug, including but not limited to the product name, use, description, and at least two samples of the product (including packaging, instructions, inserts, etc.). The firm should explain the issue they found with the product, how they found this issue, and also the reason the issue occurred. For example, if the firm finds a leaking pipe near a product assembly line and tests for batches of the drug produced on that line are positive for contamination, they would submit that as the reason for how they believe their products came to be affected. After submitting a field report, the potential risks will be assessed.

2. Processing and tracking

In processing the recall, a Health Hazard Assessment will be conducted by the regulatory body to determine the recall class (defined above). Level, notification, directions, mechanics, impacts on the economy, and the individual consumer must all be considered in determining recall strategy. The level of recall refers depends upon the part of the distribution chain to which the recall is extended (wholesale, retail, pharmacy, medical user, etc.). Notification is the way consumers are alerted to the recall. In cases of a severe risk, a media release should be promptly issued. The regulatory body recommends a written notification, so consumers will have lasting documentation. There are guidelines for notification depending on type; these types include mail, phone, facsimile, e-mail, media. Instructions and mechanics are data provided to the buyer regarding suitable action for the recall. The instructions embrace if the product is to be returned, and if so, how and where they must return the product. It is important to consider the recalled drug's place in the market, should the recall lead to market shortages.

3. Compliance and reporting

The Regulatory body will conduct an Effective check to determine the success of the recall. The drug will either undergo controlled destruction or reconditioning (i.e. relabeling with the correct label). Status reports are conducted throughout the recall to determine effectiveness.

The root cause of the recall must be addressed and corrected to prevent future occurrences. After all corrective action is acknowledged and carried out, the Regulatory body can terminate the recall.

The firm has to submit an interim report to the recall co-ordination committee within 2 weeks and a final report should be furnished within 30 days. These reports may include details on the cause of recall, the extent of distribution, effectiveness of the recall, corrective actions implemented, method of destruction of recalled products [2-4,10].

B) Post- recall procedure

The firm has to submit an interim report to the recall co-ordination committee within 2 weeks and a final report should be furnished within 30 days. These reports may include details on the cause of recall, the extent of distribution, effectiveness of the recall, corrective actions implemented, method of destruction of recalled products [4].

- ✓ **Recall terminated -** A recall will be terminated when the regulatory authorities determine that all reasonable efforts have been made to remove or correct the violated product in accordance with the recall strategy, and when it is appropriate (reasonable) to assume that the product subject to the recall has been removed and or correction has been made equivalent with the degree of hazard of the recalled product. Written notification that a recall is terminated will be issued by the appropriate Division office to the recalling firm.[7]
- ✓ **Recall completed** - For monitoring purposes, the regulatory authorities classify a recall action "Completed" when all outstanding products, which could reasonably be expected is recovered, impounded, or corrected. Some recalls may require a limited inspection at the recalling firm as a final monitoring step to verify the recall has been completed.[7]

C) Destruction of recalled products

The destruction should be carried out at a site approved by the recall committee and under the supervision of persons so designated by the recall committee. Appropriate documentation giving details of the product name (including Brand name, if any), Batch number (including date of manufacture and expiry date as given on the product) and the quantity destroyed should be maintained and signed by the persons under whose supervision the operation was done [11].

How To Minimize Product Recalls?

The drug recalls makes the pharmaceutical company's financial situation in bad condition. The reputation of the company decreases due to the recalls.

- By ensuring compliance with regulations and standards.
- By providing legal protection as well as a drug product and corporate brand protection through better response times.
- By decreasing cycle time and production/operation costs by speeding up quality and process efficiency.
- By reducing the risk of missing or incomplete data through closed-loop product recall decision-making process.
- By providing flexible yet monitored environments through fully configurable process workflows.
- By improving the quality of the product via operating processes by integrating with the best quality control systems.
- By increasing operational transparency.
- By increasing accountability through automated audit trails [6].

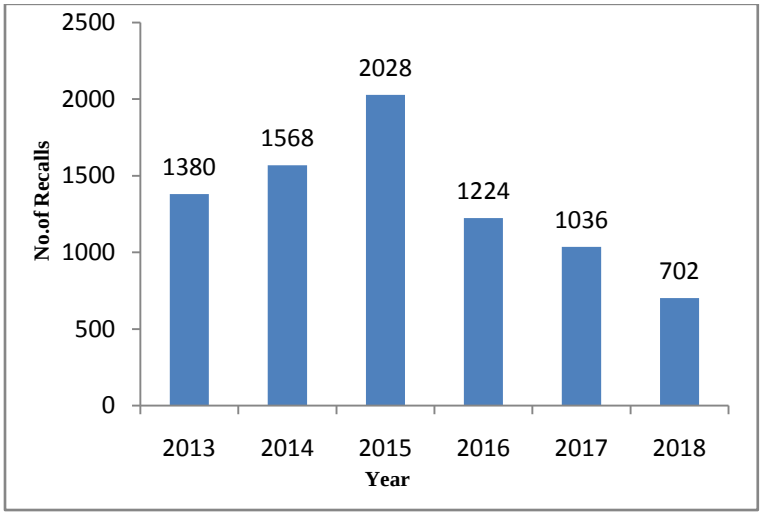

Figure 2: Number of recalls as per FDA [8,9]

A risk management program can reduce the occurrence of recalls.

The following are the strategies for managing recalls:

i) Reducing risk:

Strict quality control measures have to follow from product development onwards to prevent the recall.

ii) Assuring risk:

Find out the difficult possibilities due to which recall happens is another strategy to predict and resolve the recall issue.

iii) Transferring Risk:

The third-party, who is also involved in making the product, who is capable of share risk and to pay for the costs of a drug recall, could help to overcome recall loss [6].

Conclusion

There has been an increasing drug recalls in the number of prescribed and OTC over the last few years. The recall is usually due to the company's discovery, customer's complaint or agencies observation. The recall information usually consists of the identity of the product; overview of the failure; the amount of product produced in the distribution chain. Drug recall impacts the pharmaceutical companies as it affects the reputation of the company. The most common reason that accounts for product recall is manufacturing errors or due to improper quality parameters. This clearly defines that the production and other manufacturing conditions didn′t follow the current Good Manufacturing Practice guidelines. Another reason involves safety/efficacy create a major impact on recalls which suggests that the safety data was not appropriate, or some kind of bias was involved during drug development time. It is essential to market the product after assuring the safety and efficacy of the new intervention, by this we can minimize drug product recalls. Major drug recall list of history suggest that lots of carelessness are involved during the drug development and manufacturing period. The long list of drug recall on the FDA website is evidence that still industries are not following the standard guidelines issued by the FDA. The process of recall execution is followed by regulatory authority and firms in a very efficient manner. This execution step is effective enough to protect the consumer's health from a particular drug that requires a recall. Therefore, even after the launch of the drug in the market, it is essential to carry out post-market surveillance and investigate the drug performance in the market.

Conflict of Interest

The authors declare no conflict of interest.

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