



“Strengthening Drug Recall Systems in India: Regulatory Insights, Case Studies, and Prevention Strategies”

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1. Abstract

The process of recalling medications is an integral function of pharmacovigilance that ensures that pharmaceuticals are safe, effective, and meet quality standards. The purpose of this review paper is to summarize drug recall practices in India, including a definition of drug recalls, the purpose of drug recalls, drug recall classification, and the regulatory framework for drug recalls. This review will provide an overview of various guidelines regarding drug recalls that have been developed by different global authorities and national authorities, such as the WHO's recommendations regarding drug recalls. Additionally, different levels of recalls as well as the procedures that a drug recall follows will be presented in this review; this will include discussing many procedures involved in the actual recall process (e.g., notification to the appropriate parties, retrieval of affected drugs, etc.). The reasons for the majority of drug recalls (e.g., manufacturing defects, contamination, mislabeling, stability issues) will be described as well. Case studies of drug recalls in India will be provided as examples of the challenges faced by companies and regulators in implementing drug recalls. This review will also discuss how drug recalls can impact patients, drug companies, and the healthcare system. Lastly, this review will summarize several ways to help prevent drug recalls, including the establishment of robust quality management systems, conducting risk assessments, and improving technology in drug manufacturing. Overall, this review discusses the need for proactive solutions and appropriate regulation to reduce the incidence of drug recalls while protecting public health.

2. Keywords

Drug recall, FDA, CDSCO, GMP, Class I recall, Pharmacovigilance, Drug safety, Regulatory compliance.

3. Introduction

A drug recall is when a company must remove a batch or entire production of a drug from the market because of safety concerns or defects. If the FDA finds a violation of regulations, it orders the company to withdraw or fix the product¹. A product recall involves taking back defective or unsafe goods and compensating consumers. Drug recalls can be costly for companies because they must replace products or cover losses. The 2018 Chang Sheng vaccine incident exposed many children to risk, showing the importance of detecting drug hazards quickly, recalling products promptly, and maintaining a transparent recall process². This type of issue is identified when government analysts declare a product substandard, often supported by reports of serious adverse effects or deaths. The defect's severity and its potential harm to patients must be assessed. If a company does not comply with recall orders, legal action may follow. Therefore, companies need strong recall procedures to protect the public. Since recalls are now common, firms should adopt proper

methods to reduce their occurrence³.

4. Purpose

This review article outlines the definitions, responsibilities, and procedures involved in initiating, reviewing, classifying, auditing, and ending a drug recall. It also covers major recall cases, the reasons behind them, and strategies to prevent or reduce future recalls⁴.

5. Definitions of Drug Recall

A drug recall is an action taken by a pharmaceutical company to remove a batch or lot of a drug product from the market due to safety, quality, efficacy, or labeling issues.

1. Hazardous Nature of Drug - In 2000, many medications were recalled because they contained Phenylpropanolamine (PPA), which was found to increase the risk of hemorrhagic stroke.

2. Contaminated Ingredients - In November 2018, the FDA recalled a hypertension medicine because it was contaminated with a substance that could increase cancer risk.

3. Labelling mistakes - A drug's labeling and packaging guide consumers, so errors or misleading information can cause misuse and harmful reactions. A recall is issued if packaging or labeling mistakes are found, or if they fail to meet regulatory standards⁵.

4. Improper sealing - These issues include inadequate knurling, incorrect sealing temperature, and improper equipment settings. e.g. Hydroxyurea Capsules (Generic Name)

5. Batch over coding - Issues included insufficient ink on the printing roller, uneven ink distribution, lack of trial printing, and inadequate quality control or in-process checks. e.g. Olanzapine Tablets⁶.

6. Regulatory Framework for Drug Recalls

Between 2012 and 2023, pharmaceutical recalls related to contamination, manufacturing issues, labeling errors, out-of-specification (OOS) results, and sterility failures were analyzed. The data show a notable increase in recalls due to manufacturing issues from 2017 to 2022, likely driven by stricter regulatory standards during these years. Overall, the observations indicate that manufacturing problems and sterility failures are the most common causes of pharmaceutical product recalls.

Analysis of cGMP-related drug recalls revealed multiple categories of violations, with the most common being **process control issues, storage issues, manufacturing failures, and nitrosamine impurities**. These four categories represent the major contributors to compliance failures leading to recalls⁷. The **Food and Drug Administration (FDA)** ensures drug safety, effectiveness, and stability by regulating pharmaceutical production and use. It enforces compliance through warning letters and recalls of products that violate regulations. Recalls involve removing or correcting unsafe products and are classified as Class I, II, or III based on the level of health risk⁸.

Recall classifications include:

Class I: Class I recalls involve dangerous or defective products that can likely cause serious health problems or death. E.g. Bacterial contamination in injectables.

Class II: Class II recalls involve products that may cause temporary health issues or pose a slight risk of serious harm. E.g. Wrong dosage strength printed.

Class III: Class III recalls involve products unlikely to cause any adverse health effects⁹.that is it describes a situation where exposure to an illegal substance is unlikely to harm health. For example, A minor container defect¹⁰. E.g. Minor label typo.

7. WHO Guidelines for Drug Recall

1. **Legal and Regulatory Framework** - According to the World Health Organization, drug recall responsibility is structured at both national and company levels:

- Each country must have a **National Regulatory Authority (NRA)** to supervise and **Legal** oversee medicine

recalls.

- **Marketing Authorization Holders (MAHs)** and manufacturers are legally responsible for initiating recalls when necessary.
- A formal **recall system must be established in national laws or regulatory guidelines** to ensure proper implementation and enforcement.

In short, WHO requires a legally defined recall framework with clear regulatory oversight and defined manufacturer responsibility¹¹.

2. Recall System Requirements (GMP-Based) - The World Health Organization requires manufacturers to maintain a **written recall procedure** that clearly assigns responsibility, defines the recall decision process, ensures timely notification to authorities and supply chain stakeholders, enables batch traceability, provides for reconciliation and proper disposal of recalled products, and includes complete documentation and reporting¹².

3. Classification of Recalls (Risk-Based Approach) - The World Health Organization classifies drug recalls based on risk to public health:

Class I: Serious or life-threatening risk

Class II: Temporary or medically reversible risk

Class III: Minimal risk, unlikely to cause harm

This system ensures recalls are managed according to the level of health hazard¹³.

4. Investigation and Root Cause Analysis - The World Health Organization requires that any quality defect be promptly investigated, with a patient safety risk assessment conducted, followed by root cause analysis and implementation of appropriate corrective and preventive actions (CAPA)¹⁴.

5. Rapid Alert and International Notification - The World Health Organization operates global alert mechanisms, including the **Global Surveillance and Monitoring System (GSMS)** and Rapid Alert System, to address substandard and falsified medicines. Countries are required to notify WHO about falsified products, serious quality defects, and defective medicines distributed internationally¹⁵.

8. Common Reasons of drug recalls

1. Contamination - When a medication is contaminated, it is present with foreign materials that do not belong to it, such as bacteria or fungi, as well as some heavy metals, other types of medications. There are also possibilities of other types of foreign substances, like glass fragments, to come into contact with medical or drug products and, therefore, have a chance of being contaminating medicines.



figure 1: contamination

2. **Mislabeling (drug labeling inaccuracies)** - Mislabeling can create situations where people are misled about the nature of drugs they receive (e.g., taking medications incorrectly). Examples (of generic drug manufacturers) that have resulted in drug recall due to mislabeling include: Missing labels, Labels on incorrect medicines (e.g. ibuprofen bottle with a label reading aspirin), Inaccurate dosage or concentration as stated on the drug label, Inadequate or inconsistent representation of dosage or concentration on drug labels. Prior to taking medication, it is highly recommended that you examine it closely. The inquiry should include identifying differences in color, markings, and shape of the medication. The inquiry should also identify any inconsistencies in labeling. Lastly, if the medication you are taking is from a different generic manufacturer, it may appear different from what you are used to. So double check with your pharmacy prior to taking any medications.



figure 2: mislabeling

3. **Adverse reactions** - also known as adverse drug events refer to instances when someone has an adverse reaction or side effect to a medication. Adverse reactions are usually considered to be less predictable than side effects. Some side effects may be predictable based on studies and clinical trials involving humans or animals. Once a drug is available, thousands or even millions of new users will take the drug creating the potential for new spontaneous adverse reactions to be reported. The reasons for recalling medications because of adverse reactions are fewer than those for contamination and/or improper labeling of medications. In many instances, other preventive measures are used such as adding warning labels or restricting use of the affected medication. Examples of medications that have been recalled for adverse reactions include: loss of sense of taste or smell; brain swelling/infection; increased chances of serious cardiovascular events such as heart attacks or strokes; and many more. If you have an adverse reaction to a medication that your doctor prescribes, you should contact him or her immediately. If you would like to report an adverse reaction, you may use MedWatch which is the FDA's voluntary reporting system that allows patients to provide feedback about their experience regarding possible health or safety issues associated with their use of medical products.



figure 3: adverse drugs reactions

4. **Inadequate Product** - If a drug is inadequate, it may not function correctly, such as being unable to receive the prescription in the appropriate manner or through a defective delivery mechanism. Examples of inadequate products include: Device not delivering the drug as intended, Clogged needle on Injection Pen and Syringe, Improper bagging or voided/compromised bags A missing tampering alert Uncertainly secure adhesive within patches as mentioned above, before utilizing, always check your diluting drug for weak or damaged bags. For example, if your bag is damaged, moisture may leak into the container and harm your drug. Inhalation holders, injection pens, and nasal candles /atomizers may require priming (a trial spray) before they can be used as intended. By priming, an issue can also be identified, e.g., a blocked needle, so that the drug can be reused.



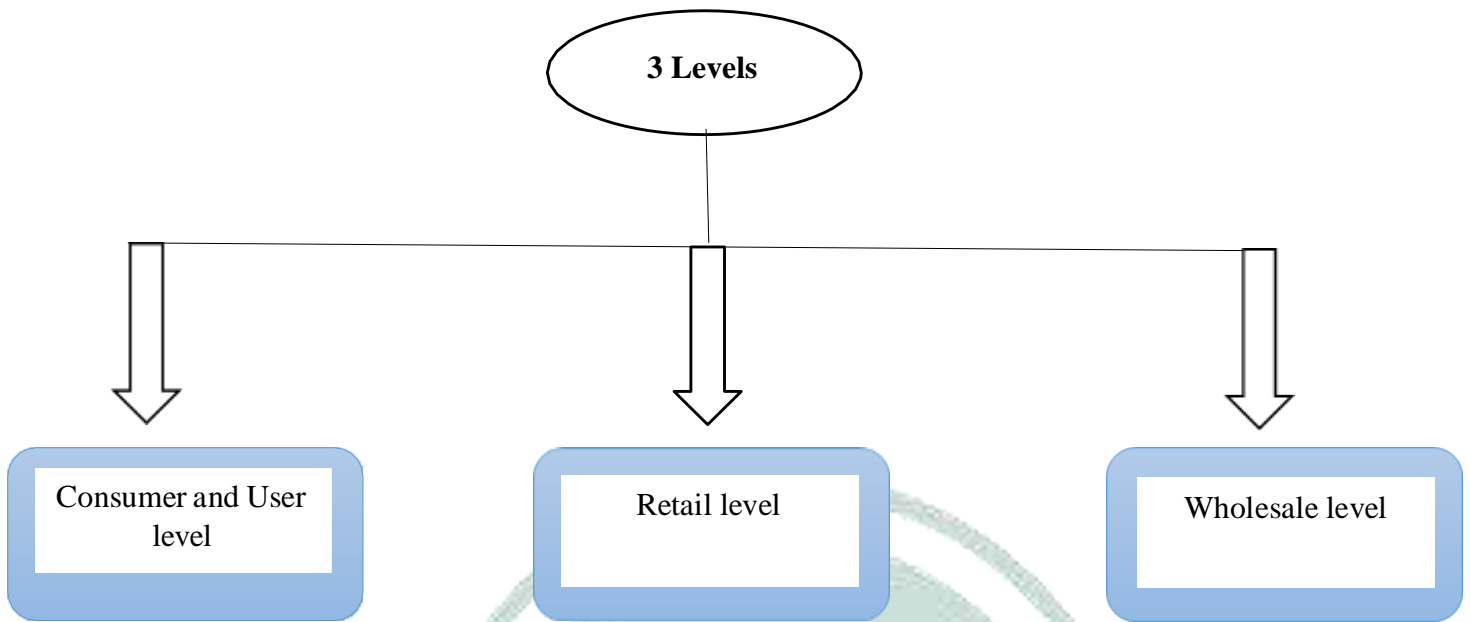
figure 4: inadequate product

5. **Incorrectly Potent** - A person who receives less than a prescribed amount of a drug will find that the drug has reduced effectiveness, while someone who receives more will be at risk of experiencing side effects. Drug manufacturers routinely test for potency as part of their quality assurance program. Recalls are likely to happen when a drug manufacturer finds sub-potent (sub-therapeutic) dosages of a drug when testing for potency. One such example is NP Thyroid, which was recalled when sub-potent NP Thyroid tablets were found during routine testing by the manufacturer¹⁶.

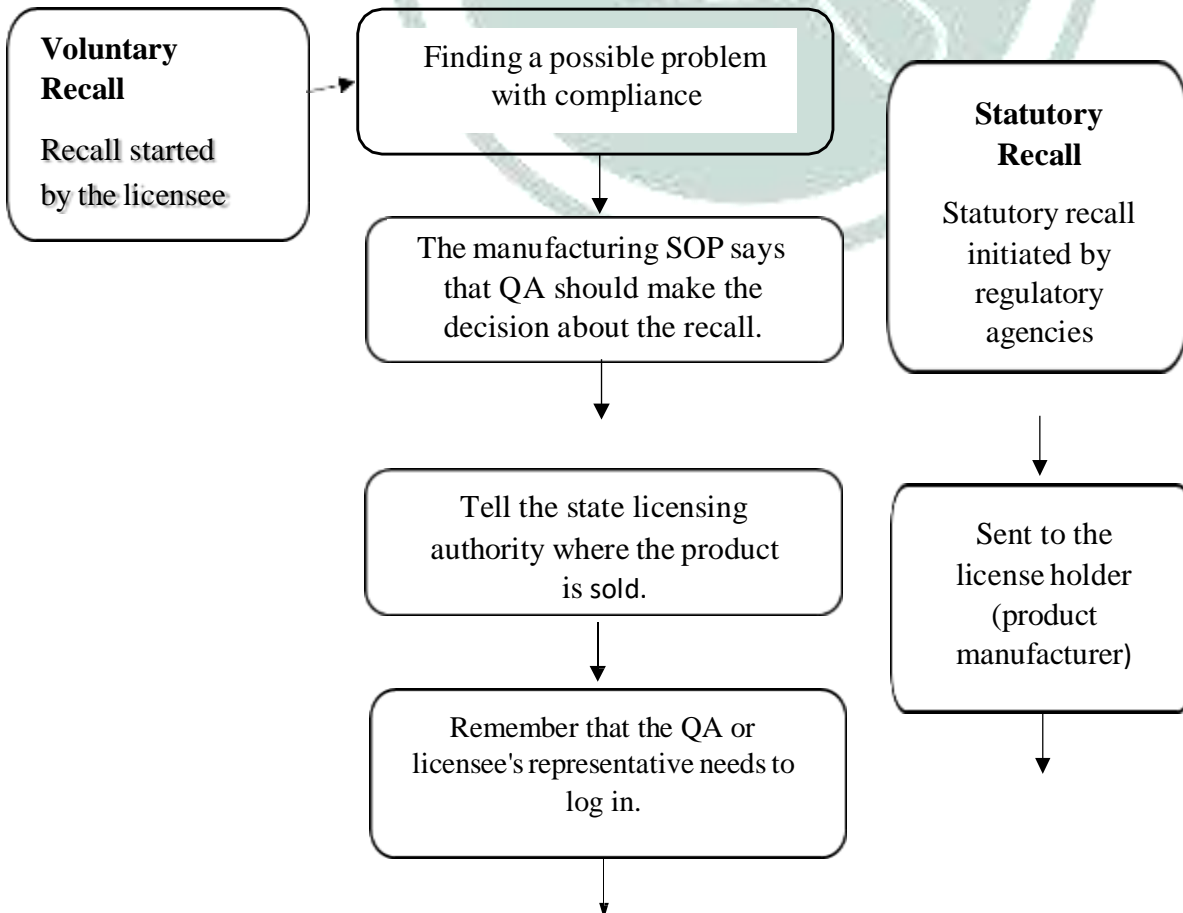


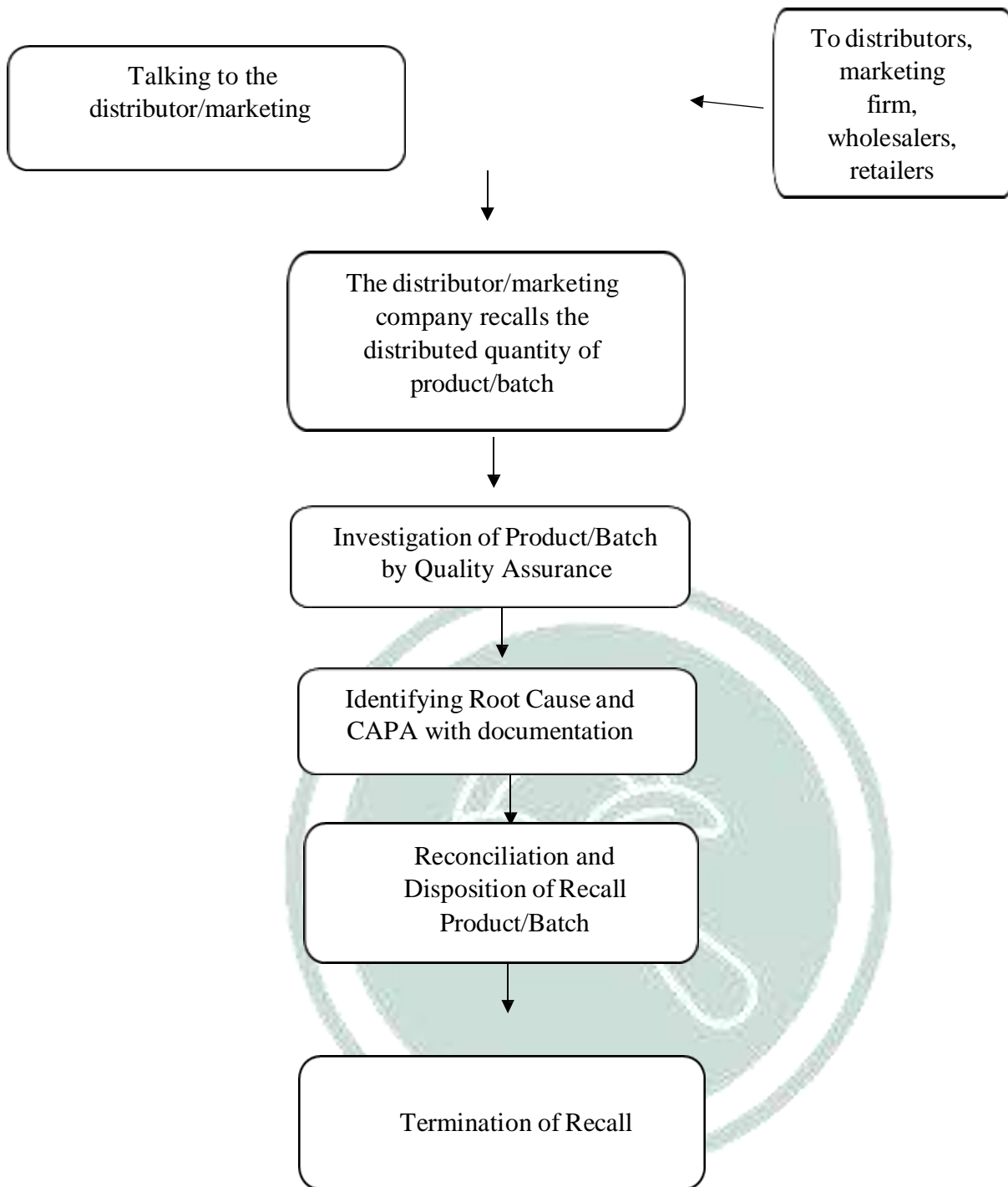
figure 5: incorrectly potent of drug

9. Levels of Recall



10. Recall Procedure





A systematic method for ensuring both the safety of patients and compliance with regulations is highlighted by the flow diagram above. When an issue is detected that may be subject to a voluntary recall (i.e., recall by the manufacturer) or a statutory recall (i.e., recall by a regulatory authority), the Quality Assurance (QA) team will assess the situation to determine whether or not to begin a recall according to their standard operating procedures (SOPs). They will notify the licensing authority of that decision. A recall log will be kept by the QA department, and notification sent to the various distributors, wholesalers, retailers, etc., advising them to halt distribution and return all affected batches. The product will then be collected from those distributors/wholesalers/retailers, and a thorough investigation will be performed to determine the root cause of the issue. Once the root cause has been identified, corrective and preventive action (CAPA) will be taken to address the issue. In addition, the entire process will be documented properly. After collection of recalled batches, reconciliation of recalled batches, proper disposal of recalled batches, the recall process will be officially closed and it will be determined that defective products have been removed from the market and future risks have been minimized.

11. Table no: 1 Case studies

Sr. No	Drug name	First Recall drug	Therapeutic type	Year	Recall class	Reason for recall
1.	Valsartan	Valsartan API	Anti-hypertensive (ARB)	2018	H2 (Class -II)	Presence of nitrosamine impurities (NDMA/NDEA-carcinogenic)
2.	Ranitidine	Ranitidine tablets	H2 receptor blocker	2019	H2	NDMA impurity (probable carcinogen)
3.	Metformin	Metformin n ER	Anti-diabetic	2020	H2	NDMA impurity above acceptable limits
4.	Ramipril	Ramipril tablets	Anti-hypertensive (ACE)	2024	H2	API sourced from unapproved vendor
5.	Bisoprolol + HCTZ	Ziac (generic)	Anti-hypertensive (β -blocker + diuretic)	2026	H2	Nitrosamine impurity contamination
6.	Injectable drugs (Emcure)	Various injections	Multiple (Antibiotic/other)	2019/2022	H2	Microbial contamination
7.	Digene (antacid)	Digene tablets	Antacid	2023-24	H3	Quality failure (NSQ drugs)
8.	Paracetamol combinations	Various brands	Analgesic/antipyretic	2024	H3	Substandard quality/counterfeit batches
9.	Rabeprazole	Rabeprazole tablets	H ⁺ /K ⁺ ATPase inhibitor (anti-ulcer)	2025	H3 (Class -III)	Failed assay and dissolution (low API content)
10.	Candesartan	Candesartan cilexetil	Anti-hypertensive (ARB)	2016	H2	Failed impurity/degradation specifications
11.	Irbesartan	Irbesartan tablets	Anti-hypertensive (ARB)	2019	H2	Impurity contamination (azido compounds)
12.	Losartan	Losartan tablets	Anti-hypertensive (ARB)	2019	H2	Azido/nitrosamine impurities ¹⁷ .

12. Impact of drug recall

1. Impact on Patients - A drug being recalled can affect a patient directly because it may result in them discontinuing a treatment regimen, particularly for chronic diseases - e.g., high blood pressure and asthma. Becoming non-compliant could create a worsening condition (or negative impact on the patient). A patient could also suffer from anxiety, lose trust in medicines, and incur additional financial burden due to replacing the recalled medication and/or requiring additional medical visits with the prescribing physician. In some cases, the recalled product might have created side effects prior to the recall, causing additional problems and a lower quality of life for the patient.

2. Impact on Pharmaceutical Companies- Pharmaceutical businesses usually incur financial losses connected with drug recalls from withdrawing their products from the market, facing potential legal liability from lawsuits or compensating for users of the recalled products, damaging their corporate image, reducing customer loyalty, leading to loss of future sales, having increased regulatory oversight with more frequent inspections, possibly losing their manufacturing licenses, in addition to the financial impact of conducting investigations into the reason for the recall and costs for corrective actions taken as a result of the recall.

3. Impact on Healthcare System- The pressure on health care systems from recalls including the increased number of hours for health care providers; More patients to be assessed and provided with alternate therapies; the possibility of complications; Increased number of drug shortages, especially when alternate therapies are inadequate, causing treatment protocols to change; Increased cost of care due to increased monitoring, hospital admission, and administrative activities; Ultimately a negative impact on efficient and reliable delivery of health care.

13. Prevention strategies

1. Quality Management System (QMS):

The best way to keep drugs from being recalled is to have a strong Quality Management System. It means following Good Manufacturing Practices (GMP), Standard Operating Procedures (SOPs), and keeping detailed records at every step of the production process. Regular internal audits, checking that processes are working correctly, calibrating equipment, and training employees all help make sure that the quality of the products stays the same. Effective testing of raw materials and qualification of suppliers lowers the risk of contamination or low-quality goods even more. A good QMS also includes Corrective and Preventive Actions (CAPA) to find the root causes of problems and stop them from happening again, which reduces the number of recalls.

2. Technological Approaches:

Advanced technologies are very important for lowering the risks of drug recalls. Automation in manufacturing cuts down on mistakes made by people and makes sure that formulations and packaging are accurate. Process Analytical Technology (PAT) and other real-time monitoring systems can help find problems during production. Serialization and track-and-trace technologies make the supply chain more open, which makes it easier to find bad batches quickly. Also, data analytics and AI can look at past production data to find possible quality problems and take steps to fix them before the products go on sale.

3. Risk Management:

Risk management is the systematic process of finding, evaluating, and controlling possible risks that come with pharmaceutical products. Tools like Failure Mode and Effects Analysis (FMEA) and risk-based quality assessments help you figure out which parts of manufacturing and distribution are most important. Companies can avoid defects that could lead to recalls by using risk mitigation strategies early in the product lifecycle. Continuous monitoring, pharmacovigilance, and post-marketing surveillance also help find problems with quality or adverse effects quickly, so that action can be taken right away and the effects of possible recalls are lessened.

14. Conclusion –

Drug recall management requires strong coordination, strict adherence to guidelines, and continuous monitoring to ensure patient safety. With the rising number of recalls each year, regulators and pharmacovigilance systems must remain vigilant and enforce compliance among pharmaceutical companies. Proper disposal of recalled products is also crucial to prevent environmental and public health risks. Companies play an important role by conducting mock recalls, internal audits, and inspections to identify and correct manufacturing defects early. Despite progress by agencies like

the U.S. FDA and EMA, challenges such as GMP violations and contamination issues (e.g., in valsartan, metformin, and ranitidine) persist, especially in developing systems like India's, where enforcement and reporting are still evolving. Strengthening GMP practices, improving recall systems, adopting advanced technologies, and promoting global regulatory harmonization are key steps to reducing drug recalls and ensuring safer medicines.

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