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Review Article

From Risk to Resilience: Uncovering Drug Recall Trends and Bolstering Safety Strategies

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ABSTRACT

The process of officially calling something back to its original or initial location is termed as "recall." Pharmaceutical recalls involve requesting to get back a product after it leaves the manufacturer to reach the distributor, retailer, or consumer. In place of the discovery of defect that affects the quality safety and efficacy of the product. Drug product recalls occur due to various reasons such as wrong or unapproved drugs, undeclared ingredients, contamination, incorrect information, and particulate issues. The probable risks or issues that arise due to a product recall or claims related to product liability and legal issues. A product recall should be perceived as an opportunity for the elimination of personal injury to the patient and damage to the reputation of the company products and rebuilding trust. Quality culture across the organization is a means of product recall prevention. In this comprehensive analysis, we delve into the drug recall statistics spanning the fiscal year 2018 to 2023 (up to July), focusing on the distinct challenges posed by recalls attributed to a lack of sterility assurance and those due to impurity profiles. Unveiling critical insights, the study highlights the impact of these issues on the pharmaceutical industry's commitment to ensuring the safety and quality of drug products. This unique analysis presents a call to action for collaborative efforts between regulatory authorities, manufacturers, and healthcare professionals. Emphasizing the value of transparent communication and proactive measures, we explore avenues to mitigate recalls and reinforce public trust in pharmaceutical products. By drawing insights from past incidents, the industry can forge a path towards a safer, more reliable future, where drug recalls due to sterility and impurity issues become rare occurrences. Swift and thorough recalls are vital to ensure patient safety. The rising trend in recalls, caused by company discovery, customer complaints, or FDA observations, impacts sales, customer relations, and supply chains. Recalls involve planned actions, including depth of recall, public alerts, and effectiveness checks.

Keywords: Recalls, Sterility, Impurity, Public health, Observations.

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INTRODUCTION

The Food and Drug Administration (FDA) regulates pharmaceutical production, development, and usage by establishing rules and regulations to ensure safety, efficacy, and stability. The FDA's enforcement actions include sending warning letters and notices of noncompliance to pharmaceutical firms. When the drugs are recalled due to concerns about their stability, safety, or efficacy, the FDA produces an enforcement report. Recall is a process of eliminating or altering products that violate the regulations of the FDA. Recalls are voluntary steps made by suppliers and producers to protect the general public's health and well-being against items that pose possible safety vulnerabilities, are fraudulent, or are otherwise faulty.[1]

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Recall means a firm's removal or correction of a marketed product that the FDA considers to violate the laws it administers and against which the agency would initiate legal action, e.g., seizure, Injunctions and Criminal Prosecution. The recall does not include a market withdrawal or a stock recovery.[2] The FDA assigns a numeral classification i.e., I, II, and III to recalls to indicate the extent to which the recalled product poses a health risk.

- **Class I-Most serious safety-related**

Circumstances wherever there is a substantial likelihood that one is being used or exposed to an unlawful product that would result in significant adverse effects or death.

For example, A label mix-up of a lifesaving drug.

- **Class II-Urgent safety-related**

A situation where the use or consumption of a forbidden substance could lead to temporary or medically treatable adverse

health effects, or where the probability of significant negative health consequences is unlikely.

For example, A drug that is under-strength but is not used to treat life-threatening situations.

- **Class III-Lowest risk**

Circumstance in which encountering or utilizing an illegal substance is improbable to adversely affect one's well-being.[3]

For example, A minor container defect.

Enforcement Report

Typically, recalls overseen by the administration are included in the Enforcement Report once they have been categorized. However, if the FDA believes that a company's actions in removing or modifying distributed products meet recall criteria, they might inform the company before formal classification. Following a hazard assessment by the FDA, the Enforcement Report section related to recalls will be adjusted to reflect the recall's classification. The recall details in the Enforcement Report can be accessed through the weekly report release, advanced search options, and an Application Programming Interface (API). Various methods are available for accessing recall information. The Enforcement Report Navigation and Definitions page offers guidance on navigating the report, utilizing the API, and understanding report contents.[4]

Recall Enterprise System

The Center for Drug Evaluation and Research (CDER), which is responsible for evaluating and researching drugs, has analyzed numerous drug recalls recorded in the FDA's Recalls Enterprise System (RES). During this analysis, they have identified instances where the data about the responsible firms is either incomplete or contradictory. Such gaps or discrepancies in information have the potential to cause delays and mistakes when identifying the firms accountable for problematic drugs, including opioids. Moreover, this situation can also result in inaccurate prioritization when routinely monitoring these sites.

The FDA has undertaken improvements to the RES process intending to achieve improved accuracy, thoroughness, and uniformity in identifying details about Responsible Firms, site scoring, and general recall information. These enhancements will empower the FDA to exercise more efficient supervision over the pharmaceutical sector, concentrating on firms identified as accountable for recall reasons. As a result of these efforts, the CDER will be better equipped to promptly and effectively implement actions specific to recalls, thus safeguarding consumers from potentially harmful products that violate regulations.[5] RES project implementation timeline in Figure 1.

According to 21 CFR part-7 subpart C

21 CFR Part-7, subpart C includes Recall policy, Health hazard evaluation and recall classification, Recall strategy, Food and Drug Administration-requested recall, Firm-initiated recall, Recall communications, public notification of recall, Recall status reports, Termination of a recall, and General industry guidance.[6]

21 CFR Section 7.40: Recall policy

The recall is a proactive step taken by distributors and manufacturers to withdraw or rectify consumer goods that violate FDA regulations, safeguarding the well-being of the public. It acts as a substitute for legal actions initiated by the FDA to remove non-compliant products. Recalls can be initiated voluntarily by the company or at the FDA's request, and in cases where a recall proves ineffective or is rejected by the company, a seizure may be employed. Recalls are typically favored over seizures, especially when products have been widely distributed.[7]

21 CFR Section 7.41: Health hazard evaluation and recall classification

A committee of FDA scientists will assess health risks associated with a product under recall or consideration, considering factors like existing diseases or injuries, potential clinical situations, impact on various population groups, severity, likelihood, and consequences of hazards. Based on this, the FDA will classify recalls as Class I, II, or III to show the level of health risk for the product in question.[8]

21 CFR Section 7.42: Recall strategy

Recall strategies are created for FDA-requested and firm-initiated recalls, considering factors such as health hazard assessment, product recognition, visibility of defects, market presence, and ongoing supply of essential items. The FDA can review and offer recommendations for changes to the firm's plan, but the recall can begin even before FDA approval. The strategy encompasses recall depth (consumer, retail, wholesale), public alerts (general or specialized media), and effectiveness checks to ensure proper notification at different recall levels (A to E).[9]

21 CFR Section 7.45: Food and Drug Administration-requested recall

The head of the FDA or an appointed representative can request a firm to commence a recall upon the determination that a distributed product poses a risk of illness, injury, or consumer deception, and the firm has not taken action. The firm will receive a written notification specifying the violation, health hazard classification, recall strategy, and instructions. The firm may be asked to provide additional information related to the recall upon agreeing to the request.[10]

21 CFR Section 7.46: Firm-initiated recall

A company can independently withdraw or rectify a product it believes to be violative. If the FDA agrees, it will be considered a recall. The firm must notify the FDA with specific product information. The FDA will review the information, classify the recall, and recommend changes if needed. The firm can proceed with the removal or correction without waiting for FDA approval. If the FDA informs the firm of a violation but doesn't request a recall, the firm's action is still considered a firm-initiated recall, subject to FDA review. If the reason for removal is unclear, the firm should consult with the FDA for assistance.[11]

21 CFR Section 7.49: Recall communications

The firm initiating the recall is required to swiftly inform its relevant direct partners regarding the recall. The message must be straightforward, indicating that the product is under recall and urging an immediate halt to further distribution or use. It should offer clear guidance on managing the recalled items and include a way for the recipient to respond to the recalling firm. For Class I and II recalls, the communication should be labelled as "urgent." Recipients are obliged to comply with the instructions and, if needed, extend the recall to their recipients.[12]

21 CFR Section 7.50: Public notification of recall

The FDA will release a weekly report on new recalls, including classification (FDA-requested or firm-initiated) and actions taken. Public notification of certain recalls may be delayed to avoid patient anxiety. It won't cover product removals or corrections deemed as market withdrawals. The report includes other regulatory actions and can be requested from the Office of Public Affairs.[13]

21 CFR Section 7.53: Recall status reports

(a) The company conducting the recall is required to provide regular status reports to the FDA district office to evaluate the progress. These reports should be submitted every 2 to 4 weeks. (b) The recall status report should include the following:

- Notified consignees and date/method of notification.
- Responding consignees and product quantities on hand at recall communication.

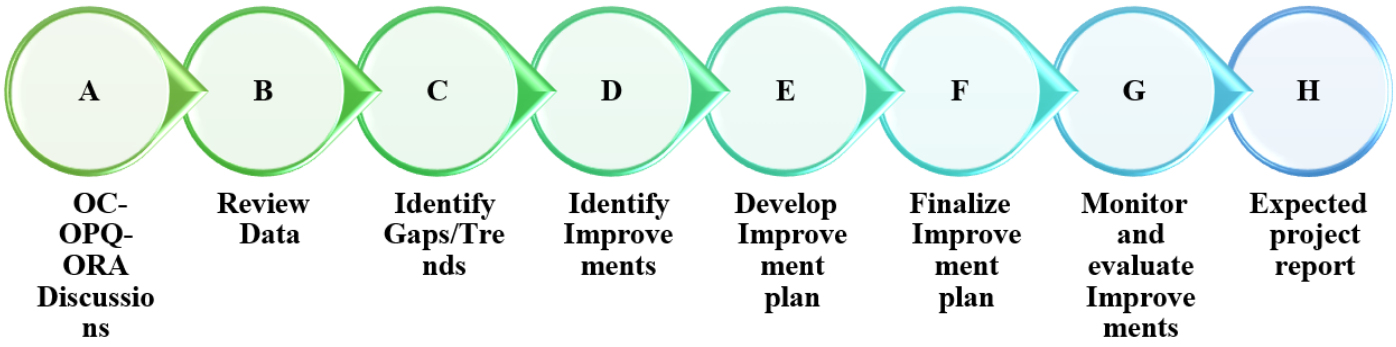

Figure 1: RES Project Implement Timeline.

Table 1: Comparison between Product Recall and Market Withdrawal.

Product Recall	Market Withdrawal
A product recall is a voluntary or mandatory action initiated by a manufacturer, distributor, or retailer to remove a product from the market. This action is typically taken when there is a significant safety issue or defect in the product that poses a risk to the consumer. Product recalls are often issued in response to reports of injuries, illnesses, or property damage associated with the use of the product. The goal of a recall is to remove defective or potentially dangerous products from circulation and provide remedies such as repairs, replacements, or refunds to affected consumers.	A market withdrawal, also known as a product withdrawal, is another Measure adopted by a company to withdraw a product from the market. However, the key difference is that a market withdrawal typically happens when a product possesses a minor flaw or does not comply with certain quality standards but is not considered to be an immediate safety risk. Market withdrawals are generally initiated by the company itself as a precautionary measure to address quality issues, labeling errors, or other non-compliance concerns. The company may remove the product from store shelves or distribution channels, but it does not necessarily involve a formal public notification or extensive consumer actions like a recall. In the end, a product recall is a more serious action taken when there is a significant safety issue with a product, while a market withdrawal is a precautionary measure usually related to quality concerns or non-compliance that do not pose an immediate safety risk. Both actions aim to address issues with products but differ in severity and the level of risk associated with the product.[17]

- Nonresponding consignees (if requested by FDA).
- Returned/corrected products by each consignee and quantity.
- Number and results of effectiveness checks.
- Estimated recall completion time frames.
- Reports end when FDA terminates the recall.[14]

21 CFR Section 7.55: Termination of a recall

The FDA concludes a recall when the product is effectively removed or rectified as per the recall plan, and the associated hazard is resolved. Written notice is sent to the recalling company.

The company that initiates the recall can request the conclusion of the recall by submitting a written appeal that meets the requirements outlined in (a), accompanied by the latest report on the recall's status and information about how the product has been handled.[15]

21 CFR Section 7.59: General industry guidance

To minimize disruptions during a recall, a prudent firm should:

- Maintain a documented contingency strategy for starting and managing recalls.
- Employ accurate coding for clear identification of valid lots and convenient recall of non-compliant batches.
- Retain distribution records beyond the product's shelf life and usage duration to meet regulatory retention mandates.[16]

Are product recall and market withdrawal being same?

The data related to product recall and market withdrawal is given in Table 1.

Does social media accelerate recalls?

Social media has emerged as a crucial channel for expressing experiences related to products, which can expose not only flaws in products but also compel companies to respond more swiftly than in the past.

By utilizing data from both the drug enforcement reports of the Federal Drug Administration (FDA) and information gathered from online forums and Twitter, our study examines the potential of social media to expedite the process of product recalls, specifically focusing on drug recalls.[18] General procedures on drug recall that are impacted by social media are shown in Figure 2.

Recall Procedures

Any batch of a product that does not satisfy the established quality criteria must be withdrawn from the market. In India, the recall procedure for drugs is managed by the Central Drugs Standard Control Organisation (CDSCO), which is the national regulatory body for cosmetics, pharmaceuticals, and medical devices. When a drug is found to have quality or safety issues, the CDSCO can initiate a recall process. The recall can be either voluntary, initiated by the manufacturer, or statutory, initiated by the CDSCO or the Drug Regulation Section of the Ministry of Health and Family Welfare.[19] The recall process involves several steps that is followed by Central Drugs Standard Control Organization (CDSCO) in India and USFDA were given in Figure 3a and 3b.

Voluntary recall: Voluntary recalls are initiated by the company itself if any occurrence that impacts the efficacy, safety, and quality of the batch/product in issue, such as

If the lot was recognized as it was non-compliant with regulations while conducting the post-marketing studies, a voluntary recall can be initiated.

If the entire lot is discovered to be faulty throughout the market complaint inquiry.

When any or all odd observations are made during the ocular examination of retention sample results that suggest an impact on the quality of the product following inquiry.

If the reports of post-marketing studies show that the product poses a substantial safety risk.

Statutory recall

Statutory recalls can even be initiated as a result of a directive or otherwise order issued by the Central or State Regulatory Authorities in one or more of the following situations:

To withdraw a drug product or lot that has been suspected of breaking the law, such as not meeting acceptable quality standards, and so on.

To recall the prohibited medications.

Illegally labelled or marketing supplies.

Product, Rule 106 violation (Diseases listed in Schedule J).[20]

Europe

The European Medicines Agency (EMA), previously known as the European Agency for the Evaluation of Medicinal Products (EMEA), serves as a decentralized scientific institution within the European Union. Its primary role is to evaluate and oversee medicinal products to safeguard and advance public and animal health. The EMA operates based on Article 47 of Directive 2001/83/EC for human medicinal products and Article 51 of Directive 2001/82/EC for veterinary medicinal products.

The European Directorate for the Quality of Medicines and HealthCare (EDQM) is a division of the Council of Europe rooted in the Convention on the Elaboration of a European Pharmacopoeia. Its expert committee has developed scientific

metrics to assess pharmaceutical care quality in Europe. The EDQM's standards are outlined in the European Pharmacopoeia, recognized worldwide as a scientific benchmark, and legally binding within EU member states. Published in English and French and regularly updated, the European Pharmacopoeia is a consistent reference for official European quality standards.

Through joint funding from the European Commission and the Council of Europe, the network of Official Medicines Control Laboratories (OMCLs) was established. This network, along with participants from the European Pharmacopoeia Convention, ensures uniform pharmaceutical product quality across Europe. The EMA takes on the responsibility of ensuring the safety of medicinal products and has the authority to enforce recalls or returns of hazardous products that have already reached consumers. It can also enforce market withdrawals to prevent the distribution, display, and offering of dangerous products to consumers.[21] Comparison between USA and Europe was given in Table 2.

Reasons for Pharma Product Recalls

Hazardous Nature of Drug

Risks linked with the medicine are frequently revealed after it has been released onto the market. It happens at this point when manufacturers become aware of the drug's effects. In 2000, for example, an enormous number of medications were recalled because they raised the risk of haemorrhagic stroke in the brain due to the presence of Phenylpropanolamine (PPA). In such

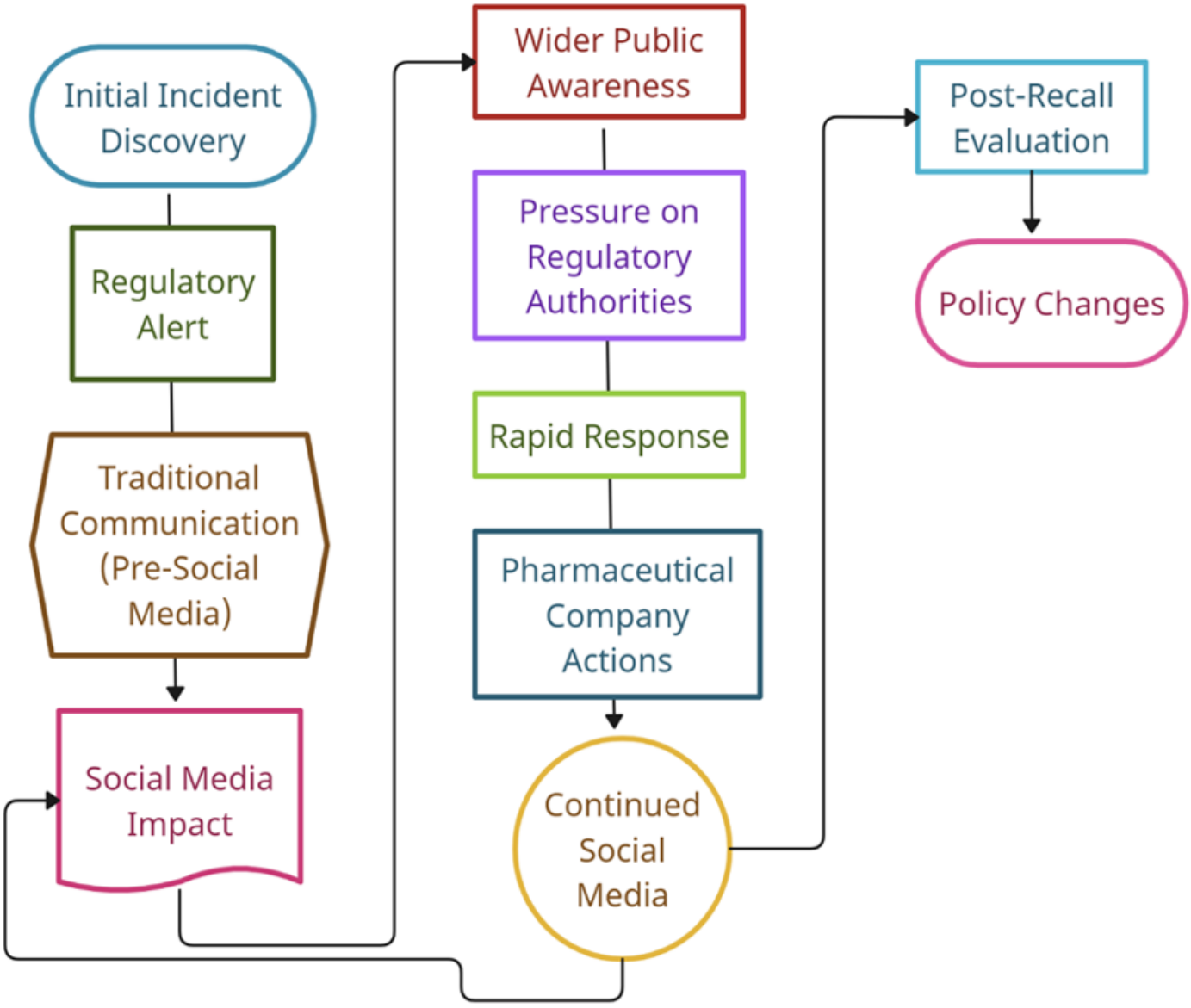

Figure 2: Social media impact on Drug Recalls general procedure.

Table 2: Comparison of Guidelines for a Drug recall established by USA and Europe.

Recall procedure	USA	Europe
Definition of Recall	The recall is a firm's removal or correction of a marketed product that the FDA considers to violate the laws it administers, and against which the Agency would initiate legal action.	Recall means any measure aimed at achieving the return of a dangerous product that has already been supplied or made available to consumers by the producer or distributor.
Regulatory Authority	United States Food and Drugs Administration (USFDA).	European Medicines Agency (EMA).
Legal Requirements	21 CFR Part 7, Subparts A and C; 21 CFR Part 107, Subpart E; 21 CFR Part 1270 - Human Tissue PHS Act - 42 U.S.C. 262.	Article 40 of Directive 2001/83/EC and Article 44 of Directive 2001/82/EC is required under Article 13(1) of Directive 2003/94 and Article 13 of Directive 91/412/EC.
Recall Initiation	Recall initiated by the manufacturer at their discretion, recall initiated by the FDA's request, or recall mandated by the FDA.	Voluntary or at the request of the competent authorities by Article 8(1)(f).
Classification of Recall	Class I, II, and III.	Class I, II, and III.
Health hazard evaluation	By the Health Hazard Evaluation Committee.	Relative health hazards associated with the use or exposure to the recalled product.
Termination of Recall	Written notification of termination to the recalling firm.	NA
Recall Strategy	The company initiating the recall must carry out the recall following an authorized recall plan.	NA
Notification and Public Warning	Informs the company, issues a press statement, posts on the FDA's website, if necessary, notify other federal and state entities, and communicates with foreign governments when needed.	Notification by the European Commission.
Recall Timeline	Recall schedule provided by the Consumer Response Unit (CRU) based on the specific product requiring recall.	Not Defined
Monitoring and Auditing the Recall	Establishes a recall assessment initiative.	The effectiveness of recalls is periodically evaluated and documented.

circumstances, the agencies request that the medicine be recalled from the market.

Contaminated Ingredients

Sometimes the production of medicine exposes its contents to contaminated by undesirable or toxic chemicals, which can elicit responses in the end-user and constitute a health concern. The FDA recalled a hypertension medicine in November 2018 owing to contamination with a risk of causing cancer.[22]

Manufacturing flaws

Defects or errors in a medicine's manufacturing process may threaten the safety and efficiency of the medicinal product. The root cause of a drug error might range from pharmacological heterogeneity between drug batches or between generic and originator pharmaceuticals to the inclusion of contaminants. If manufacturers do not follow the appropriate Health Authority's GMP rules, they may be asked to recall the product.

Labelling mistakes

A drug's labeling and packaging serve as guidance for end consumers. Any labeling error or misleading message may lead to a patient misunderstanding, resulting in an unpleasant response. A recall is made if a mistake is discovered in the packaging or labeling, or if it is not following the HA standards. Due to mismatched instructions, a major pharmaceutical company was forced to recall its fever treatment for children last year.[23]

Levels of Recall

The decision regarding the extent of a product or lot recall is determined by considering the categorization of the recall and the extent of its distribution. At the Consumer/User Level, the scope varies depending on the nature of the product and may include interim wholesale or retail stages. This encompasses individual customers, patients, physicians, and healthcare facilities. The Retail Level, which is just before the consumer or user level,

encompasses entities like retail supermarkets, pharmacies, hospital pharmacies, dispensing physicians, clinics, nursing homes, and similar organizations. Wholesale Distribution includes all stages of the supply chain between the manufacturer and the merchant.

For Class I recalls, the recall should encompass wholesale/ distributor, retail, and consumer levels. In such cases, public notifications need to be disseminated through various media channels like newspapers, television, radio, and others. Class II recalls should be executed up to the wholesale and retail levels. Class III recalls should be executed up to the wholesale level.[24]

Overview of Drug Recall Statistics

During the six years from fiscal year 2018 to 2023 (up to July), the pharmaceutical industry witnessed several significant drug recalls. These recalls encompassed a wide range of medications, including prescription drugs, over-the-counter products, and dietary supplements. By delving into the numbers, we can acquire a deeper comprehension of the magnitude and impact of drug recalls during this period.

Recall Frequency

This data, which was collected from the USFDA, shows that the number of Drugs that are recalled varies from year to year. Here is a summary of data on drug recalls by fiscal year in the last six years. The statistics of drug recalls from 2018-2023 are depicted in Figure 4a.

Fiscal Year 2018

During 2018, the maximum number of drugs recalled are related to class II, this indicates that moderate risk to patient health. Common reasons for these recalls include manufacturing defects, labeling inaccuracies, and contamination concerns. A total of 1206 drugs are recalled.

Fiscal Year 2019

In 2019, there was a substantial increase in drug recall incidents in the pharmaceutical industry, with 1877 recalls reported. Most of the recalls acquired a Class II classification, indicating a moderate risk of harm to patient health. The primary causes leading to the recalls were related to manufacturing flaws, labeling mistakes, and contamination worries.

Fiscal Year 2020

In the Year 2020, drug recall events declined due to improved quality control measures implemented by pharmaceutical companies. Class II recalls remained a concern, however, due to their indication of severe health risks. A total of 1490 drugs were recalled during the period because they posed risks of adverse side effects or life-threatening complications.

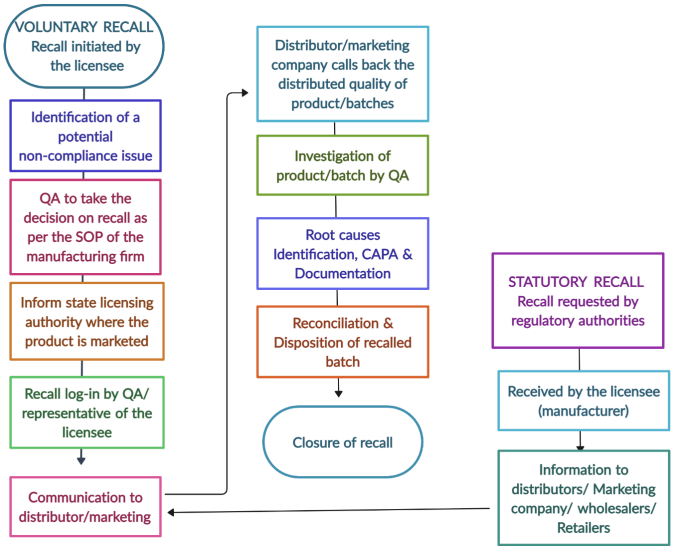

Figure 3a: Recall Process of drugs as per CDSCO.

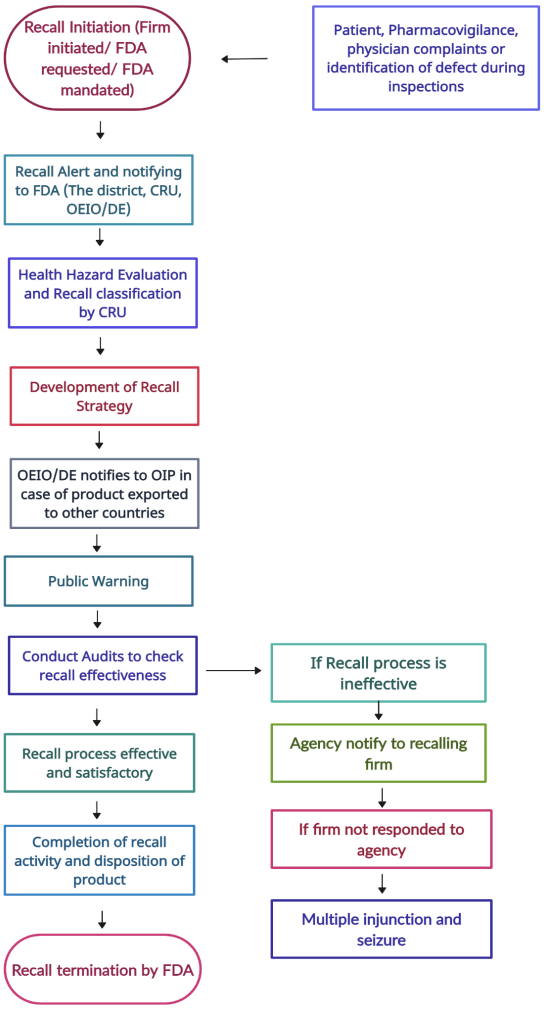

Figure 3b: Recall process of drugs as per USFDA.

Fiscal Year 2021

This fiscal year saw a decline in drug recall events, attributed to pharmaceutical companies implementing improved quality control practices. Nonetheless, Class II recalls, which involved severe health risks, continued to be a concern. Notable recalls included those related to adverse side effects or life-threatening possibilities. During this period, a total of 891 drugs were recalled.

Fiscal Year 2022

In this current financial year, there has been a significant increase in the number of drug recall incidents within the pharmaceutical sector. This surge can be attributed to improvements in monitoring systems and stricter regulatory oversight. Most of the recalls were labeled as Class II, indicating a moderate level of risk to patient well-being. Manufacturing defects, labeling inaccuracies, and contamination concerns were the main factors behind these recalls. A total of 1552 drugs have been recalled.

Fiscal Year 2023(up to July)

During this year there is 941 drugs are recalled. The maximum number of drugs are related to Class II, indicating a moderate risk to patient health.[25]

The statistics of recalled products by classification are shown in Figure 4b. Statistics of recall Events by fiscal year from 2018-2023(July) seen in Figure 4c. Statistics of recall events by classification are given in Figure 4d, and Statistics of recall events by status are seen in Figure 4e.

Recall Events

3 types of events are as follows:

Ongoing Recall Events

Ongoing recall events refer to situations where a recall has been initiated by a company or regulatory authority, but the recall process is still in progress. This means that the affected products are actively being removed from the market, and the company is still in the process of notifying relevant parties and taking necessary corrective actions.

Terminated Recall Events

Terminated recall events occur when a recall initiated by a company or regulatory authority, is concluded before all affected products have been removed from the market. This may happen if the company determines that the risk associated with the recalled products has been adequately addressed, or if the recall process is no longer feasible or necessary.

Completed Recall Events

Completed recall events refer to situations where a recall initiated by a company or regulatory authority, has been fully executed, meaning that all affected products have been removed from the market, and necessary corrective actions have been implemented.[26]

Lack of Assurance of Sterility

The main cause of recalls in the previous six years was sterility problems. Mainly because of inadequate manufacturing and the integrity of container closures, sterility problems arise during the production process. The greatest option to reduce the microbial burden is terminal sterilization, which can reduce recalls owing to lack of sterility. From 2018-2023, 2900 drugs are recalled due to this reason. By supplying life-saving drugs, the pharmaceutical industry plays a crucial role in enhancing global health. However, recent pharmaceutical product recalls prompted by hygienic issues have brought attention to a troubling issue: the industry's general lack of assurance of sterility. Product recalls in the pharmaceutical sector have significantly increased recently, raising questions about the reliability of cleanliness in the production processes. Maintaining cleanliness is important for pharmaceutical production since it ensures the security and potency of drugs. This article examines the causes of these recalls, their possible effects, and the urgent need for better procedures to maintain public trust while ensuring cleanliness and patient health.

The Significance of Sterility in Pharmaceuticals

Maintaining sterile conditions is crucial while producing pharmaceuticals. The safety and efficacy of drugs can be impacted by even minute levels of bacteria. The primary goals of maintaining sterility throughout the production process are to avoid contamination and safeguard patients from dangerous bacteria, fungi, and other diseases. By maintaining this sterility, pharmaceutical companies work to offer safe and efficient therapies.[27]

Understanding the Causes of Sterility Concerns

Pharmaceutical product recalls can occur for several reasons, such as problems with product efficacy, quality, or safety. The inability to guarantee sterility is an important factor in recalls. Addressing the various issues that contribute to this lack of sterility is essential, some of them include:

Manufacturing Process Complications

The complexity of pharmaceutical manufacturing processes poses challenges to maintaining sterility. Human error, equipment malfunctions, and inadequate sterilization practices can lead to contamination and compromise product sterility. The intricacies involved in large-scale production increase the likelihood of errors, underscoring the need for stringent quality control measures.

Table 3: List of few recalled drug products due to lack of assurance of sterility in the last 6 years.

Sl. No.	Recalling firm name	Product classification	Status	Reason for recall	Date (m-d-y)	Product Description
1.	Pharmedium Services, LLC	Class II	Terminated	Lack of sterility assurance.	02/20/2018	"Dexamethasone Sodium Phosphate added to 0.9% Sodium Chloride in all strengths, all doses, and all packaging".
2.	Vitalab Pharmacy, Inc	Class II	Terminated	Lack of sterility assurance.	05/09/2018	"Methionine 25 mg/Inositol 50 mg/Choline 50 mg/ Cyanocobalamin 1 mg/mL, Sterile injectable".
3.	Guardian Pharmacy Services	Class II	Terminated	Lack of sterility assurance.	08/08/2018	"B-Complex Rx only. packaged in a) 100 mL bag b) 100 mL MDV vial".
4.	Pharm D Solutions, LLC	Class II	Terminated	Lack of sterility assurance.	11/01/2018	"Oxytocin 30 unit in LR 500 mL 0.06 units/mL".
5.	First Pharma Associates LLC	Class II	Ongoing	Lack of sterility assurance.	07/11/2019	"Prostaglandin 20 µg/mL/ Procaine 0.1% Injection, packaged in a) 2.5 mL and b) 10 mL vial".
6.	Pfizer Inc.	Class II	Terminated	Lack of sterility assurance.	07/12/2019	"Milrinone Lactate Injection 200 µg (0.2 mg)/mL* in 5% Dextrose Injection, 20 mg/100 mL, 100 mL bag, Rx Only".
7.	"First Royal Care Co. LLC, dba Red Mountain Compounding Pharmacy"	Class II	Terminated	Lack of sterility assurance.	11/05/2019	"S-VIT B COMPLEX INJ SOLN (HP); Rx Only, 30ML glass vial".
8.	Altaire Pharmaceuticals, Inc.	Class II	Ongoing	Lack of sterility assurance.	11/15/2019	"Ofloxacin Ophthalmic Solution, USP, 0.3%, 5 mL".
9.	Pfizer Inc.	Class II	Terminated	Lack of sterility assurance.	03/05/2020	"Elelyso (taliglucerase alfa) for injection, 200 units/vials".
10.	Imprimis NJOF, LLC	Class II	Ongoing	Lack of sterility assurance.	12/30/2020	"Dexamethasone - Moxifloxacin PF Injection (1/5) mg/mL, Imprimis Rx Volume: 1 mL/vial".
11.	BIOTA Biosciences LLC	Class II	Terminated	Lack of sterility assurance.	06/19/2020	"Sterile Cannabidiol (CBD) 4mg/mL, 10 mL vial".
12.	Innovative Intrathecal Solutions, Inc. dba Innovative Compounding Pharmacy	Class II	Ongoing	Lack of sterility assurance.	04/06/2020	"Hydroxyprogesterone Caproate (BUD) 350 mg/mL, 4 mL, Injectable"

Sl. No.	Recalling firm name	Product classification	Status	Reason for recall	Date (m-d-y)	Product Description
13.	Teva Pharmaceuticals USA	Class II	Ongoing	Lack of sterility assurance.	02/21/2021	"Desmopressin Acetate Injection USP, 4 µg/mL, 1 mL Preserved Vial (NDC 0703-5051-01), packaged in 10X1 mL Vials per Tray".
14.	Glenmark Pharmaceuticals Inc., USA	Class II	Ongoing	Lack of sterility assurance.	09/21/2021	"Arformoterol Tartrate Inhalation Solution 15 µg/2 mL For Oral Inhalation Only Rx".
15.	Pfizer Inc.	Class II	Completed	Lack of sterility assurance.	12/02/2021	"5% Dextrose Injection, USP, 50 mL ADD-Vantage Unit, Rx only".
16.	First Royal Care Co. LLC, dba Red Mountain Compounding Pharmacy	Class II	Terminated	Lack of sterility assurance.	10/26/2021	"PYRIDOXINE HCL (B6) 100 mg/mL MDV, Red Mountain Compounding Rx".
17.	CIPLA	Class II	Ongoing	Lack of sterility assurance.	07/20/2022	"Difluprednate Ophthalmic Emulsion, 0.05%, 5 mL bottles, Rx only".
18.	Pine Pharmaceuticals, LLC	Class II	Terminated	Lack of sterility assurance.	09/15/2022	"Bupivacaine HCl 0.375% w/v and Lidocaine HCl 2% w/v Solution for Retrobulbar or Peribulbar Injection".
19.	Akorn, Inc.	Class II	Completed	Lack of sterility assurance.	03/24/2022	"TheraTears Extra (sodium carboxymethylcellulose) 0.25% Lubricant Eye Drops, 30 Sterile Single-Use Vials per box".
20.	Teva Pharmaceuticals USA	Class II	Ongoing	Lack of sterility assurance.	01/13/2022	"Norepinephrine Bitartrate Injection USP 4 mg/4 mL (1 mg/mL), 4 mL Single-Dose Vials, 10 vials per carton, Rx Only".
21.	Pfizer Inc.	Class II	Ongoing	Lack of sterility assurance.	01/05/2023	"Heparin Sodium 2,000, USP Units, per 1,000 mL (2 USP Units/mL) in 0.9% Sodium Chloride Injection, 1,000 mL bags, a) Case (NDC 0409-7620-59), b) Single Unit (NDC 0409-7620-49), Rx only".
22.	Apollo Care, LLC	Class II	Ongoing	Lack of sterility assurance.	05/18/2023	"VANComycin 1.5g added to 250 mL of 0.9% Sodium Chloride Injection, Rx only".
23.	Sentara Infusion Services	Class II	Completed	Lack of sterility assurance.	02/15/2023	"Ampicillin/Sulbactam 3 g IN NS 100 mL, antibiotic, Rx only".
24.	Sentara Infusion Services	Class II	Completed	Lack of sterility assurance.	02/15/2023	"Diphenhydramine 18 mg in 3.6 mL NS SYRINGE, antihistamine, Rx Only".

Inadequate Environmental Controls

Maintaining a controlled environment is essential for preventing contamination during pharmaceutical production. Cleanrooms, air filtration systems, and proper gowning protocols are crucial components. Inadequate maintenance of these systems, insufficient monitoring, and improper training of personnel can result in compromised sterility, leading to product recalls.

Inadequate Quality Control Systems

The absence or inadequacy of robust quality control systems within the manufacturing process significantly contributes to the lack of sterility assurance. Insufficient testing protocols, incomplete environmental monitoring, and ineffective validation of sterilization methods increase the risk of contamination, compromising the overall sterility of pharmaceutical products.

Supply Chain Vulnerabilities

The pharmaceutical supply chain is extensive and complex, involving multiple stages from raw materials to finished products. The lack of assurance of sterility can arise from weaknesses in supply chain management, including substandard storage and transportation conditions, inadequate validation of suppliers, and inconsistent quality control measures at each stage. Contaminated ingredients or materials can compromise the sterility of the final product, necessitating recalls.

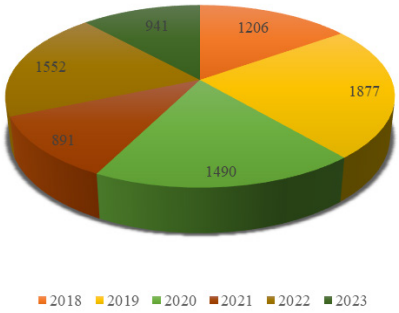

Figure 4a: Number of drugs recalled in the last 6 years by US FDA.

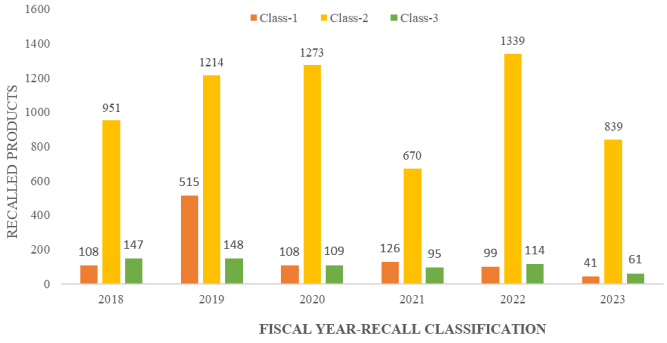

Figure 4b: Number of drugs recalled in last 6 years by USFDA based on classification.

Inadequate Regulatory Oversight

While regulatory agencies enforce strict guidelines and standards, gaps in oversight can contribute to the lack of assurance of sterility. Insufficient inspections, limited resources, and outdated regulations can hinder the identification and prevention of sterility issues. Strengthening regulatory frameworks and enhancing collaboration between industry and regulators is crucial to addressing this challenge effectively.[28] Some of the examples of recalled drug products due to lack of sterility assurance from 2018-2023(July) are included in Table 3.

Key practices for reducing the likelihood of a positive sterility test result

Testing Standards

Adherence to testing standards should be strictly followed to ensure proper sterility. This includes timely laboratory testing and frequent environmental monitoring. It is critical to adhere to certain protocols to reduce the chances of obtaining a positive sterility test result and to guarantee the purity of pharmaceutical products. The protocols comprise:

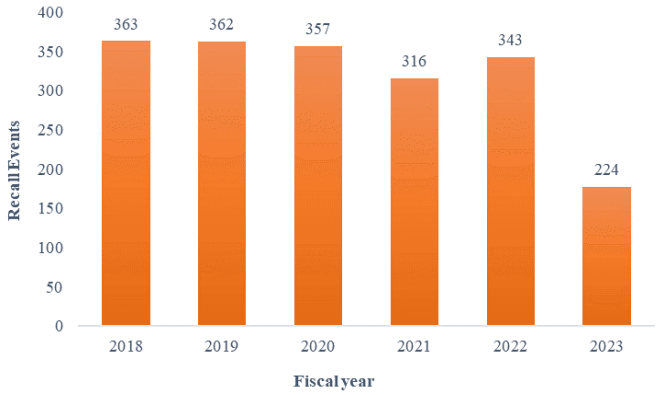

Figure 4c: Statistics of recalled products by recall events from the last 6 years.

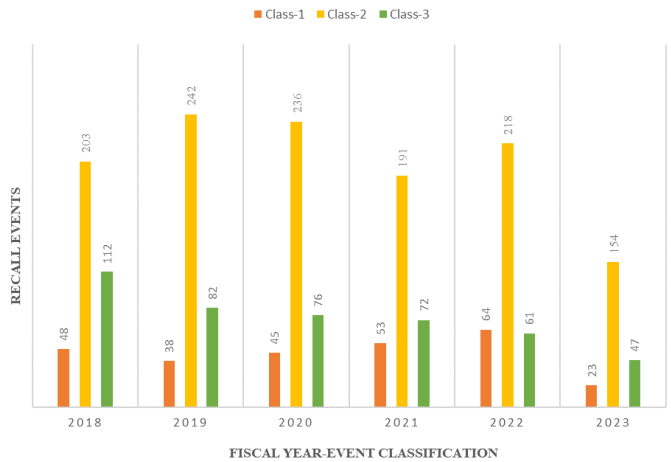

Figure 4d: Statistics of recalls data by classification.

Maintaining an Aseptic Environment

It is necessary to preserve a sterile atmosphere all through the compounding and manufacturing process. This necessitates the use of sterile devices and materials and appropriate hand hygiene.

Providing Personnel Training Everyone participating in the compounding activity should be provided with adequate preparation. This comprises schooling them in sterile techniques, gown methods, hand washing, and manners that foster cleanliness in the clean room, intending to lessen the probability of contamination.

Designing and Maintaining the Cleanroom

The cleanroom where compounding takes place should be designed and maintained and should meet the established criteria. This includes filtration of the air, management of particle quantities, and ensuring proper airflow.[29]

Environmental Surveillance

Regularly checking the environment of the cleanroom is extremely important to pinpoint any conceivable sources of contamination. Taking samples from the air and surfaces to identify microbial contamination and making sure the cleanroom fulfills all microbial requirements are part of this surveillance.

Validation and Certification

It is critical to confirm and certify the apparatus, procedures, and sterilization techniques to guarantee they can usually produce sterile products. This includes automatically testing the sterilization supplies and safeguarding the sterility cycles are productive.

Sterilization Techniques

Equipment, containers, and parts used in compounding should all be sterilized according to the correct procedures. Depending on the demands of the product, this may involve methods like steam sterilization, dry heat sterilization, or filtration.[30]

Quality Control and Assurance

To monitor and confirm the efficacy of the compounding procedures, appropriate quality control and assurance programs need to be in place. This is to implement the finished products through testing, keeping careful monitoring of the process parameters, and doing frequent audits.

Documentation and Record-Keeping

To track and trace each stage of the compounding process, accurate and thorough documentation is essential. Record-keeping for batches, cleaning and maintenance tasks, data from environmental monitoring, and any deviations or corrective measures done are all included in this.[32]

Supplier Evaluation

Making ensuring that the raw materials and components are trustworthy, high-quality, and reliable is essential. To make sure incoming supplies fulfill the required requirements, suppliers must be assessed, and relevant testing and verification must be performed on them.[31]

Continuous Training and Improvement

Regular training programs and initiatives for continuous improvement should be implemented to keep employees updated on best practices and identify areas for process enhancement.[32]

By implementing these essential procedures, the risk of a positive sterility test outcome can be minimized, and the production of sterile pharmaceutical products can be ensured.

Case Study: 1

All sterile compounded drugs product from Ranier's Rx Laboratory that are still within their expiration dates are being voluntarily recalled. Hospitals and consumers are also affected by this recall. Concerns about potential sterile product contamination as a result of pharmacy procedures are what led to this recall. These issues were discovered by the FDA during a regular examination. It is crucial to emphasize that there have been no patient complaints or adverse events associated with this recall. Additionally, the pharmacy's compounded medicinal items have not been linked to any complaints of adverse occurrences to the FDA. Furthermore, there is no proof that the sterile medicinal goods that have been recalled are genuinely tainted However, the pharmacy has decided to start the recall as a preventative action to set patient safety first.

The recall specifically pertains to sterile medicinal products distributed from January 17, 2018, to July 10, 2018, that remain within their expiration dates. These products were solely supplied and distributed directly to patients and medical facilities within Pennsylvania. Importantly, it should be emphasized that neither This recall does not affect the non-sterile compounded products or the retail pharmacy activities of the pharmacy.[33]

Case Study: 2

Sagent Pharmaceuticals, Inc. has issued a voluntary recall of four batches of Levetiracetam Injection, USP. This recall applies to all users across the country. The reason behind the recall is the identification of issues with the integrity of the container closures in reserve sample vials. This concern could potentially lead to the presence of non-sterile products. It's crucial to acknowledge the potential risks associated with using an intravenous product that's intended to be sterile but may not be. Such use could result in severe systemic infections that pose a life-threatening risk. So far, there have been no records of grievances or negative occurrences associated with this issue at Sagent Pharmaceuticals. Levetiracetam Injection, USP 500 mg per 5 mL, is employed

for treating particular seizure types and is typically contained within a single-use vial of 5 mL. Further information includes Levetiracetam Injection USP, with lot numbers along with their time of expiration, BOG85VB (June 2022), BOK88VA (September 2022), BOK89VA (September 2022), and B1G194A (June 2023), all sharing the NDC number 25021-780-05. The product was distributed nationwide from March to November 2021.[34]

Impurity Profile

Over the past six years, impurity-related recalls in the pharmaceutical industry have been instances where certain drugs or pharmaceutical products were removed from the market due to the discovery of unwanted substances or impurities in them. These impurities exceeded the acceptable limits set by regulatory agencies to ensure patient safety and product quality. These recalls were initiated to protect consumers from potential health risks and maintain the integrity of pharmaceutical products. Pharmaceutical companies have been working diligently to improve quality control measures and adhere to regulatory guidelines to minimize the occurrence of such recalls and ensure the safety of their products. 545 Drugs have been recalled due to impurity in the last 6 years.

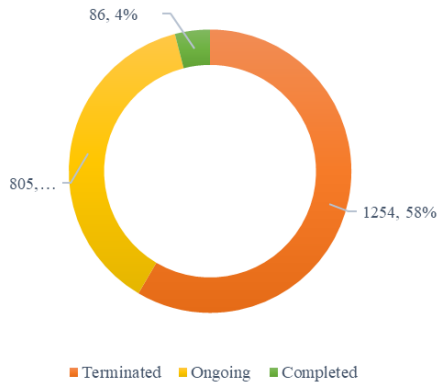

Figure 4e: Statistics of recalls data by status.

Some of the examples of recalled drug products due to Current Good Manufacturing Practices (CGMP) Deviations-Impurity profile from 2018-2023 (July) are included in Table 4.

Understanding CGMP Deviations

Impurities are any unexpected chemicals detected in medicinal products. The impurity profile of a drug product is a detailed description of all such contaminants that are present in the product. The production, testing, and control criteria for these pharmaceutical items are broken down under CGMP rules. However, a mismatch in these profiles might result in product recalls, which may be caused by a variety of factors, such as manufacturing process deviations from the approved CGMP standards some of which are:[35]

Equipment malfunctions

Deviations from CGMPs may result from improperly calibrated, maintained, or verified manufacturing equipment. Defects in the production process caused by such breakdowns might result in impure or inferior goods.

Inadequate documentation practices

Accurate and thorough documentation is essential to the integrity of the manufacturing process. Without correct documentation, there is a risk of compromising the quality of the products and making it difficult to trace them. Errors and deficiencies in the documentation, such as missing batch records, and not recording revisions or deviations, may lead to a lack of accountability and responsibility along the chain, leading to lower quality standards.[36]

Table 4: List of a few recalled drug products due to Impurity in the last 6 years.

Sl. No.	Recalling firm name	Product classification	Status	Reason for recall	Date (M-D-Y)	Product Description
1.	Mylan Pharmaceuticals Inc.	Class II	Ongoing	The FDA's laboratory analysis has confirmed the existence of an impurity called N-nitrosodiethylamine (NDEA) in the Active Pharmaceutical Ingredient (API).	12/14/2018	"Amlodipine 10 mg Valsartan 320 mg, 30-count bottle".
2.	"Aurobindo Pharma Limited (Unit I)"	Class II	Terminated	CGMP Deviations: Identification of NDEA (N-Nitrosodimethylamine), a cancer-causing impurity, found in the active substance.	10/31/2018	Irbesartan Bulk Active Pharmaceutical Ingredient.
3.	Hetero Labs Limited Unit V	Class II	Completed	CGMP Deviations: Detection of a cancer-causing impurity in the Active Pharmaceutical Ingredient (API) utilized for drug product manufacturing.	08/23/2018	"Camber Pharmaceuticals, Inc. Valsartan Tablets, USP, 40 mg, 30 Tablets Rx Only".

Sl. No.	Recalling firm name	Product classification	Status	Reason for recall	Date (M-D-Y)	Product Description
4.	Dr. Reddy's Laboratories, Inc.	Class III	Terminated	Impurity/Degradation Specifications Not Met: Out-of-Specification (OOS) result was noticed for ATV Cyclo FP Impurity and overall degradation impurities assessed at the 18-month stability interval in a batch of 500 tablets containing Atorvastatin Calcium 40 mg.	08/14/2018	"Atorvastatin Calcium tablets, 40 mg, 500-count bottle, Rx only".
5.	Aurobindo Pharma USA Inc.	Class II	Ongoing	CGMP Deviations: The FDA laboratory has verified the existence of an impurity, N-nitrosodimethylamine (NDEA), within the Active Pharmaceutical Ingredient (API) employed for product manufacturing, exceeding the interim acceptable daily intake threshold of 0.083 parts per million.	01/14/2019	"Valsartan and Hydrochlorothiazide tablets USP 320 mg/25 mg, 90-count bottles".
6.	Lupin Pharmaceuticals Inc.	Class III	Terminated	Impurity/Degradation Specifications Not Met: Out-of-Specification (OOS) outcomes identified for different individual impurity and overall impurity levels.	02/05/2019	"Bimatoprost Ophthalmic Solution 0.03%, packaged in a) 5 mL (NDC 68180-429-02) and b) 7.5 mL (NDC 68180-429-03) bottles, Rx only".
7.	Torrent Pharma Inc.	Class II	Ongoing	CGMP Deviations: Verification by the FDA laboratory established the existence of an impurity, N-nitrosodimethylamine (NDEA), in the Active Pharmaceutical Ingredient (API) employed for product manufacturing, surpassing the interim acceptable daily intake threshold of 0.083 parts per million.	02/15/2019	"Losartan Potassium Tablets, USP, 100 mg, a) 30-count".
8.	Apotex Inc.	Class II	Completed	GGMP Deviations: Possible contamination with impurity N-nitrosodimethylamine (NDMA).	11/12/2019	"Walgreens Maximum Strength Wal-Zan 150 Ranitidine Tablets, USP 150 mg/Acid Reducer 95 Tablets NDC 0363-1030-09; d) 65 Tablets NDC 0363-1030-06".
9.	Appco Pharma LLC	Class II	Terminated	CGMP Deviations: Impurity N-nitrosodimethylamine (NDMA) found in API.	01/07/2020	"Ranitidine Capsules 300 mg, 30 count bottles. Rx only".

Sl. No.	Recalling firm name	Product classification	Status	Reason for recall	Date (M-D-Y)	Product Description
10.	Denton Pharma, Inc.	Class II	Ongoing	CGMP Deviations: Presence of NDMA impurity detected in the product.	01/20/2020	"Ranitidine Tablets, USP 150 mg, a). 4 count bottle (NDC 70934-017-04), b). 20-count bottle (NDC 70934-017-20), c). 24-count bottle (NDC 70934-017-24) d). 30-count bottle (NDC 70934-017-30) e). 90-count bottle (NDC 70934-017-90)".
11.	"H J Harkins Company Inc dba Pharma Pac"	Class II	Completed	CGMP Deviations: Presence of NDMA impurity detected in the product.	01/20/2020	"Ranitidine, 150 mg Tablets, a) 7 counts, b) 14 count, c) 20 count, d) 30 count, e) 60 count; Rx, Only".
12.	Direct Rx	Class II	Terminated	CGMP Deviations: Presence of NDMA impurity detected in the product.	10/05/2020	"Ranitidine 300 mg, 30 Tabs bottles, Rx only".
13.	"Sun Pharmaceutical Industries Inc"	Class III	Terminated	Failed Impurity/Degradation Specifications.	02/09/2021	"Pantoprazole Sodium for Injection 40 mg/ vial For I.V. infusion only".
14.	Pfizer Inc.	Class II	Ongoing	CGMP Deviations: Detection of N-nitroso-varenicline impurity exceeding FDA's interim acceptable intake limit.	07/30/2021	"Chantix (varenicline) Tablets, Contains 1 Starting Week (0.5 mg* x 11 tablets), 3 Continuing Weeks (1 mg x 42 tablets)".
15.	Lupin Pharmaceuticals Inc.	Class II	Terminated	CGMP Deviations: impurity N-nitrosoirbesartan detected in API.	11/01/2021	"Irbesartan Tablets USP, 300 mg a) 30 count (NDC 68180-412-06) and b) 90 count NDC# 68180-412-09) bottles, Rx only".
16.	Ascend Laboratories LLC	Class II	Completed	Impurity/Degradation Specifications Not Met: Unspecified impurities not meeting criteria were detected in multiple batches of Cephalexin FOS USP 125 mg/5 mL.	01/04/2021	"Cephalexin for Oral Suspension, USP, 125 mg per 5 mL, packaged as a) 100 mL (when mixed) bottle, NDC 67877-544-88; b) 200 mL (when mixed) bottle NDC 67877-544-68, Rx Only".

Sl. No.	Recalling firm name	Product classification	Status	Reason for recall	Date (M-D-Y)	Product Description
17.	Pfizer Inc.	Class II	Ongoing	CGMP Deviations: The presence of N-nitroso-quinapril and N-nitroso-hydrochlorothiazide impurities exceeds the permissible daily intake threshold.	04/06/2022	"quinapril HCl/ hydrochlorothiazide tablets, 20 mg/12.5 mg*, 90 Tablets bottles, Rx Only".
18.	Lupin Pharmaceuticals Inc.	Class II	Terminated	CGMP Deviations- AZIDO Impurity levels observed to be above acceptable limits.	05/03/2022	"Losartan Potassium and Hydrochlorothiazide Tablets USP, 50 mg/12.5 mg a) 30-count bottles (NDC# 68180-215-06) b) 90-count bottles (NDC# 68180-215-09), Rx Only".
19.	Mylan Institutional, Inc. (d.b.a. UDL Laboratories)	Class II	Ongoing	Impurity/Degradation Specifications Not Met: Out-of-Specification (OOS) outcome observed for a different individual impurity at the 12-month room temperature interval.	05/11/2022	"Esomeprazole Magnesium Delayed-Release Capsules, USP 40 mg, packaged in Unit Dose Blister Cards of 6 (10 cards of 6 Capsules each per carton), Rx only".
20.	Preferred Pharmaceuticals, Inc.	Class II	Terminated	CGMP Deviations- AZIDO Impurity levels observed to be above acceptable limits.	05/24/2022	"Losartan Potassium & HCTZ Tablets 50mg/12.5 mg, hydrochlorothiazide USP 12.5, Pkg Size: 90, NDC: 68788-7758-09".
21.	Sun Pharmaceutical Industries Inc.	Class II	Ongoing	The impurity (Deacetyl Diltiazem Hydrochloride) did not meet specifications in stability testing, and dissolution testing at the FDA laboratory was unsuccessful.	02/02/2023	"Diltiazem Hydrochloride Extended-Release Capsules, USP, 360 mg; Rx only; 90-count bottles".
22.	Aurobindo Pharma USA Inc.	Class II	Ongoing	Failed Impurities/Degradation Specifications: The firm's investigation due to customer complaints for discoloration found that the product was out of specification for an impurity.	05/24/2023	"Pain Reliever, Acetaminophen USP Caplets, 500 mg, 225-count bottles packaged in a cardboard carton".

Sl. No.	Recalling firm name	Product classification	Status	Reason for recall	Date (M-D-Y)	Product Description
23.	Sun Pharmaceutical Industries Inc	Class III	Ongoing	Failed Impurities/Degradation Specifications: Above the specification, limits yielded for related substance norepinephrine sulfonic acid impurity during routine product monitoring.	04/10/2023	"Norepinephrine Bitartrate Injection, USP, 4 mg/4 mL* (1 mg/mL), 4 mL Single-dose Fliptop Vial (NDC 47335-615-40); packaged in 10 x 4 mL Single-dose Fliptop Vials per carton (NDC 47335-615-44)".
24.	Lannett Company Inc.	Class III	Completed	Failed Impurity/Degradation Specifications.	01/16/2023	"Triamterene and Hydrochlorothiazide Capsules, USP (37.5 mg/25 mg), Rx Only, 1000 Capsules per bottle, Distributed by: Lannett Company, Inc., Philadelphia, PA 19136.NDC: 0527-1632-10".

Contamination and cross-contamination

Impurities can enter the final product if contamination is not controlled throughout the production process. Cross-contamination, which happens when pollutants from one product are transmitted accidently to another, may affect the quality and safety of several items.[37]

Addressing CGMP Deviations and Impurity Profiles

To mitigate CGMP deviations and prevent impurity-related recalls, pharmaceutical manufacturers should prioritize the following:

Robust quality management systems

Implementing complete quality management systems that include adequate equipment maintenance, rigorous documentation practices, and significant quality control methods will assist in avoiding and detecting CGMP deviations.

Effective risk management

Through the use of risk assessment methods, risks related to impurity development and contamination may be identified and mitigated, helping to minimize deviations and lessen the chance of recalls.[38]

Adequate process validation

Effective validation of procedures assures that manufacturing processes are well-defined, regulated, and capable of producing products that satisfy predefined quality requirements consistently. This involves testing for pollutants and defining acceptable levels for their presence.

Continuous improvement and training

The significance of compliance, accurate documentation, and good manufacturing practices should be emphasized and employees' awareness of CGMP rules may be improved by regular training and education programmes.[39]

Case Study 1

Lupin Pharmaceuticals Inc. has made the voluntary decision to recall all available Metformin Hydrochloride Extended-Release Tablets USP in 500mg and 1000mg strengths that have been distributed to consumers. After continuous assessment and ongoing communication with the FDA, further analysis has revealed that specific batches of the medication have exceeded the acceptable limit for N-Nitrosodimethylamine (NDMA), an impurity. As a precautionary measure, Lupin Pharmaceuticals has opted to recall all lots of the mentioned Metformin tablets across the United States. As of now, no adverse events related to this recall have been reported.[40]

Case Study 2

Precision Dose Inc. is initiating a voluntary recall of five batches of Ranitidine Oral Solution, USP 150 mg/10 mL, aimed at consumers. The recall is being conducted due to the possibility of the levels of N-Nitrosodimethylamine (NDMA) exceeding the thresholds established by the FDA. This action is prompted by

the manufacturer's (Amneal Pharmaceuticals, LLC) recall, which included the batches that were reprocessed by Precision Dose Inc.[41]

DISCUSSION

Recalls are vital processes employed to mitigate potential risks to public health and safety by removing or correcting products from the market. These procedures, often guided by regulatory frameworks like 21 CFR Part 7 Subpart C, involve a structured approach encompassing identification, notification, and corrective actions, as well as in Europe the EMA ensures medicinal product safety and has authority over recalls of hazardous products, while the EDQM, through the Official Medicines Control Laboratories network, maintains uniform quality standards across Europe. The Recall Enterprise System (RES) facilitates effective management, enhancing coordination during recalls. Social media significantly accelerates recalls by swiftly disseminating information to a broader audience and fostering rapid responses. Pharma product recalls can stem from diverse reasons, including contamination, labeling errors, quality concerns, or safety issues. The recall procedure typically unfolds in stages: initiation, assessment, execution, and closure. Classification into recall levels, ranging from Class I (high risk) to Class III (low risk), determines the urgency and extent of the recall. Though specific drug recall statistics from 2018 to mid-2023 would require current data, issues like lack of sterility assurance or unexpected impurities in pharmaceuticals can trigger recalls, emphasizing patient safety as paramount.

CONCLUSION

In conclusion, the drug recall statistics from the fiscal year 2018 to 2023 (up to July) paint a concerning picture of the challenges faced by the pharmaceutical industry in ensuring the safety and quality of drug products. Recalls resulting from a lack of sterility assurance and impurity profile issues highlight critical areas that demand immediate attention and improvement. The prevalence of recalls due to a lack of sterility assurance serves as a clear and strong illustration of the significance of stringent manufacturing practices and the necessity for maintaining aseptic techniques throughout the production process. Ensuring the absence of harmful microorganisms is fundamental to preventing potential infections and safeguarding the health and well-being of patients who rely on these medications for treatment. Likewise, drug recalls attributed to impurity profiles underscore the significance of robust quality control measures and thorough testing at every stage of drug development and production. The identification and prompt resolution of impurities are essential to mitigate health risks and preserve patient trust in the pharmaceutical industry. These statistics call for collective action and collaboration between regulatory authorities, manufacturers, and healthcare professionals to implement proactive measures and ensure product safety. By learning from past incidents, embracing rigorous manufacturing standards, and fostering transparent communication, the pharmaceutical industry can work towards reducing drug recalls, enhancing patient safety, and upholding the highest standards of quality in delivering medications to patients worldwide. Only through continuous improvement and unwavering commitment to patient welfare can we strive for a future where drug recalls due to sterility and impurity issues become rare occurrences.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

FDA: Food Drug and Administration; **RES:** Recall Enterprise System; **CFR:** Code of Federal Regulations; **EMA:** European Medicines Agency; **EMEA:** European Agency for the Evaluation of Medicinal Products; **CGMP:** Current Good Manufacturing Practices; **NDMA:** N-Nitrosodimethylamine; **API:** Application Programming Interface.

SUMMARY

The drug recall statistics from 2018 to mid-2023 reveal concerns in the pharmaceutical industry quality and safety. Recalls due to sterility and impurity issues highlight the need for strict manufacturing and quality control. Preventing infections and maintaining patient trust require robust measures. Collaboration among regulators, manufacturers, and healthcare professionals is vital. Learning, adherence to standards, and transparent communication can reduce recalls and ensure safe medications. Continuous improvement is crucial for minimizing future sterility and impurity-related recalls and prioritizing patient well-being.

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