ANALYZING THE IMPACT OF DRUG-RELATED INCIDENTS ON HEALTHCARE SYSTEMS AND POLICY: A SYSTEMATIC REVIEW OF INCIDENTS AND TRAGEDIES CAUSED BY DRUG-RELATED EVENTS AND THEIR IMPACT ON HEALTHCARE POLICY, REGULATION, AND PRACTICE

*Flydon Melrick Picardo[1], Rishabh Suryawanshi[2], Devarakonda JayaLakshmi[3], Shreyas HL[4], Aparna Anil Bharde[5], Dr. B Lakshmi[6], V Sai Kishore[7]

[1]*MBA, Department of Pharmaceutical Management, NIPER Hyderabad, Telangana, India*

[2]*MBA, Department of Pharmaceutical Management, NIPER Hyderabad, Telangana, India*

[3]*MBA, Department of Pharmaceutical Management, NIPER Hyderabad, Telangana, India*

[4]*MBA, Department of Pharmaceutical Management, NIPER Hyderabad, Telangana, India*

[5]*MBA, Department of Pharmaceutical Management, NIPER Hyderabad, Telangana, India*

[6]*Assistant Professor, Department of Pharmaceutical Management, NIPER Hyderabad, Telangana, India*

[7]*Assistant Professor, Department of Pharmaceutical Management, NIPER Hyderabad, Telangana, India*

Corresponding author

Email ID: flydonpicardo.niperh2022@gmail.com

ABSTRACT

Drug-related incidents refer to any events that occur due to the use of contaminated, adulterated, spurious or defective drugs as well as events occurring due to medication errors and adverse drug effects. Such issues are rising globally at exponential pace. These incidents are resulting in side effects Due to the presence of a suspected cancer-causing contaminant, the US Food and Drug Administration (FDA) recalled numerous blood pressure drugs in 2018. Ranitidine, a drug used to treat heartburn, was recalled in 2019 because it may contain a human carcinogen. Due to the presence of methanol, which can be hazardous when consumed or absorbed via the skin, hand sanitizers were recalled in 2020.Contamination-related drug recalls can greatly impact the pharma industry and the general health of the public. Drug recalls can potentially damage people and generate financial losses for drug producers and distributors. Drug recalls can occasionally result in a scarcity of life-saving medications. Public health and safety are seriously at risk when drugs are recalled owing to contamination. Numerous medicine recalls resulting from contamination have recently been brought to light, along with their possible effects on patients and the pharmaceutical business. Developing countries like India has faced lots of issues with the quality of medicine drawing eyeballs from nations across the world. Working cooperatively to avoid and handle contamination-related drug recalls is crucial for regulatory authorities, drug producers, and healthcare providers.

INTRODUCTION

As a result of higher inspection rates, the introduction of modernization and the digital world into the industry, and an alarming rise in the number of recalled pharmaceutical products,regulatory agencies and public health officials are focusing on tighter regulations to prevent further recalls of faulty pharmaceutical products **(Burrows VK,2010)**.

In recent years, there have been a number of prescription recalls because of subpar quality, The main reasons for these recalls were related to issues such as bad taste, color variation, poor packaging, low therapeutic efficacy, and other quality-related concerns

The FDA declared that it is urging that producers remove all OTC (over-the-counter) and prescription ranitidine medications using the market at this time.

This is the most recent advancement in continuing study on the contaminant N-Nitrosodimethylamine (NDMA), which is present in medications containing ranitidine (usually sold under the brand name Zantac). Due to this emergency market withdrawal request, products containing ranitidine won't be accessible in the United States via new or existing prescriptions or for over-the-counter use ***(Fda.gov, 2020).***

Ibuprofen for infants is now being voluntarily recalled by Tris Pharma, Inc.Because of worries that they might have included an excess of ibuprofen, the pharmaceutical company withdrew batches of infant ibuprofen in December of last year.One of the original recalled products is a 0.5-ounce bottle of Ibuprofen Concentrated Oral Suspension for Infants, USP (NSAID), 50 mg per 1.25 ml ***(Healthline,2019).***

Despite claiming there was no quality issue, Abbott India has recalled one batch of the well-known thyroid disorder medication Thyronorm due to a dosage labeling error.

The mislabeled batch was invoiced in Telangana and Madhya Pradesh. Thyronorm, a medication used to treat hypothyroidism, is being recalled by Abbott owing to a labeling issue that mislabeled the dosing strength (mcg or microgram) in one batch (No. AEJ0713; Mfg. Date: March 2023) ***(Business standard, 2023)***

Poor-quality medications pose a substantial threat to public health, particularly in developing and emerging economies, and may significantly increase the clinical and financial burden on the country. The availability of intentionally counterfeit medications has received much of the attention, but patients are also receiving subpar medications as a result of poor manufacturing and quality-control procedures used to produce real medications (either branded or generic). Because they can accidentally result in healthcare failures like antibiotic resistance and the spread of disease within a community, as well as individual deaths or further illness, substandard medicines are pervasive and pose a threat to health **(Johnston & Holt, 2014)**

One of the landmarks in fight against substandard drugs in India was the Mashelakar committee report in 2003. This is a thorough report that presented recommendations for raising the drug regulation standards and policies in India to meet international standards and for addressing the issue of fake or subpar medications.

Two key recommendations are: (1) tight vigilance must be sustained, with frequent surprise pharmacy checks and for the reason checks (suspicious checks); and (2) the supply of pharmaceutical quality testing facilities. Exercises to regularly test drug samples also aid in detecting the prevalence of counterfeits.

Sun Pharma recalled 1,920 bottles of Dofetilide Capsules, a drug used for treatment of irregular heartbeat (***Business Today,*** **2023**).

Due to a possible contamination, Global Pharma Healthcare issued a voluntary countrywide recall for Artificial Tears Lubricant Eye Drops (***New Indian Express, 2023***). According to inspection reports made public by the Food and Drug Administration, federal inspectors discovered scores of problems at an eye drop company that are reportedly connected to a fatal drug-resistant bacteria epidemic. These problems ranged from unclean equipment and clothing to lacking safeguards and processes (***Telegraph India,*** **2023**).

A generic medicine intended to boost blood pressure in adult patients with acute hypotension is being recalled, according to the most recent Enforcement Report from the US health authorities (***CBS News, 2023***). Products sold in the US market by Sun Pharma and Hetero are being recalled due to production problems. Sun

Pharmaceuticals Inc recalled 16,450 vials of Norepinephrine Bitartrate Injection for "Failed Impurities/Degradation Specifications" ***(Economic Times,*****2023**).

OBJECTIVES

1. To examine the impact of drug-related incidents and tragedies on healthcare policy, regulation, and practice, including changes in prescribing practices, drug monitoring programs, and regulatory frameworks.

2. To explore the factors contributing to drug-related incidents and tragedies, including patient characteristics, healthcare provider behavior, and system-level factors such as access to care and social determinants of health.

3. To identify gaps in drug related incidents and tragedies and provide future recommendations for regulatory and policy development.

REVIEW OF LITERATURE

MAIDEN PHARMACEUTICALS AND GAMBIA

Four syrups manufactured by Maiden Pharmaceuticals Limited, a company located in Haryana, primarily utilised for cough in children, have been deemed "contaminated" and "substandard" by the WHO because they may contain hazardous and potentially lethal ingredients. Magrip N Cold Syrup, Makoff Baby Cough syrup, Kofexmalin Baby Cough Syrup, Promethazine Oral Solution are the four products mentioned by WHO in its study. ***(Business today, 2022)*** it is reported that Maiden Pharmaceuticals Limited (Haryana, India) is the company that makes these goods.

On performing laboratory investigations, ethylene glycol and diethylene glycol was found which is not used in cough syrups. It is possible that the syrup might have travelled to other countries due to unofficial markets **(World Health Organization, 2022).**

The four cough syrups developed and exported by Maiden Pharmaceuticals, which are thought to be the cause of 66 children dying in the Gambia, were of standard quality, according to the central government ***(India News,*** **2023).**

The Ranitidine case involving Maiden Pharmaceuticals, a company that sent medicines to Vietnam, started in 2013. In December 2013, the Drugs Controller General of India (DCGI) was told by the Indian Consulate General in Vietnam that the Drugs Administration of Vietnam
had banned 46 Indian enterprises for quality violations. On the list of companies that were blacklisted, Maiden Pharmaceuticals was ranked fourth. Maiden Pharmaceuticals together with its Director Naresh Goyal and Technical Director MK Sharma, were found guilty in the matter involving the poor-quality Ranitidine hydrochloride tablets BP (Mantek-150).

According to Section 27(d) of the 1940 Drugs and Cosmetics Act, Goyal and Sharma were each given a sentence of two years and six months of harsh imprisonment as well as a fine of Rs. 1 lakh apiece ***(The Tribune, 2020)***

LIFE THREATENING BACTERIA IN CANCER DRUG

A Hyderabad-based company's cancer medication was highlighted by health officials in Lebanon and Yemen as being subpar following tests on the medication. As a result of life-threatening bacteria being discovered in one of its batches, Celon Lab's methotrexate, an injectable anti-cancer medication and suppressor of immune system, has been warned against by the World Health Organisation.

The advisory warned that patients taking the injection "may have compromised immune systems and be more susceptible to opportunistic infections."

The drug may have entered Lebanon and Yemen via the unofficial markets, the WHO noted. MTI2101BAQ, the batch name, was purchased "outside the regulated supply chain" and was supposed to be sold only in India **(*Times Now,* 2023)**

The producer could not ensure the safety of the medications, according to the WHO, because they were not intended for the markets of these nations. It also raised concern that the medication may have been distributed to

other nations via purported unregulated supply networks and stressed the significance of quickly identifying and removing the drug from use

(The News Minute, 2023)

PROPOFOL FAILS QUALITY TEST

Following reports indicating that propofol did not adhere to the India Pharmacopoeia (IP) 2018 monograph or meet the quality guidelines established by the Central Drugs Standard Control Organisation (CDSCO), the Drugs Control Administration (DCA) ordered a pharma company at Kala Amb in Himachal Pradesh to stop manufacturing the contentious injection of propofol ***(The Tribune, 2022)***.An investigation consisting of drug inspectors and members from CDSCO, drew samples of the drug Propoven (Propofol injection) and sent them to regional drugs testing laboratory in Chandigarh because it was suspected that the drug had killed five patients who had undergone orthopaedic and neurosurgeries.

The drug has been labelled by the laboratory as "not of standard quality" according to the report by CDSCO. This is because it failed the tests for sterility, Ph and free fatty acids ***(Hindustan Times, 2022)***

MARION BIOTECH RUNS INTO A PROBLEM

Dok-1 Max, a syrup manufactured by Noida's Sector 67-based Marion Biotech, has been implicated in the deaths of 18 children in Uzbekistan, prompting scrutiny of the company. The business manufactures more than 100 healthcare items, along with a few OTC (over-the-counter), prescription, and herbal medications that are mostly used to treat pain, fever, and colds **(*The Firspost,* 2022*)*.** According to the business's website, Dok-1 Max Syrup contains the three medications paracetamol, guaifenesin, and phenylephrine hydrochloride, which lessen the common cold symptoms, the flu, coughing up a fever, and other infectious upper respiratory tract infections. **(*CNBC TV18*, 2023).**

The WHO gave a product alert on the two cough syrups produced by the company, Dok-1 Max and Ambronol Syrup. According to WHO, national quality control laboratories of the Ministry of Health of the Republic of Uzbekistan conducted laboratory analyses of samples of cough syrups and discovered both products contained prohibited levels of diethylene glycol and/or ethylene glycol as impurities **(*ZEE News* ,2023).** India canceled the license of the company after 22 of its drug samples were labeled spurious and adulterated **(*BBC News,* 2023)**

THE COUGH SYRUP SAGA ENTERS THE PACIFIC

The World Health Organization (WHO) reported on 25th April, 2023 that contaminated cough syrup produced by an Indian company has been discovered in the M arshall Islands and Micronesia (***Telegraph India***, **2023)**. The substandard syrup – Guaifenesin Syrup TG Syrup – was reported to WHO on April 6. The stated manufacturer of the medicines in the latest alert was India's QP Pharmachem Ltd, based in Punjab and the marketer of the product was Trillium Pharma, based in India's Haryana, the WHO said ***(MSN,* 2023).**

In response to a recent regional state pharma agency inquiry, QP Pharmachem's managing director Sudhir Pathak said that the company had analyzed a sample from the exported batch and the result was found to be satisfactory, and the regulator felt the same **(*The Hindustan Times,* 2023).**The Indian government granted QP Pharmachem authorization to export 18,000 bottles of the syrup to Cambodia exclusively. How the item got to the Marshall Islands, and Micronesia is unknown ***(The Print,2023)*.** After issuing a global call to action in January 2023 to help avoid more fatalities, WHO chief of substandard medicines Rutendo Kuwana said earlier that the organisation was working with nations to help test medications when asked to do so ***(Reuters, 2023)***.

DRUG RECALL PROCEDURE LAID DOWN BY FDA

A medicine is said to be recalled when it is taken off the market because of flaws in its quality, safety, or efficacy, or because it poses a risk to human health **(Sundaran et al., n.d.,2013)**.Recalls of prescription drugs are often voluntary actions taken by the drug manufacturers.

Companies issue recalls on their own when they realise their products are flawed or harmful. If the FDA becomes involved, it may order a recall, which businesses often comply with. The FDA may sue the producer

under the Federal Food, Drug, and Cosmetic Act to compel compliance. Companies are responsible for recalling prescription drugs and ensuring they

succeed if the FDA rejects an appeal. Generally speaking, the companies are also required to inform the FDA when a recall of a prescription drug is in progress and to provide progress reports. The FDA supervises the destruction of the hazardous prescription medicine when the recall is completed.

The FDA then launches an inquiry to determine why the prescription drug recall was required and what made the prescription drug dangerous. An FDA ad hoc committee evaluates the health risk for a product before deciding whether to recall it. The following elements are taken into account: the risk of an adverse event occurring as a result of using the product; the seriousness of the health hazard; the chance that the event would occur; and the effects of the incident. Based on these findings, the FDA classifies the recall as Class I, Class II, or Class III to reflect the relative level of health danger associated with the recalled product or the one being considered for recall.

The regulations for product recall are given in different parts of 21 CFR A public warning is released to inform people of the significant health risk the recalled product poses **(USFDA**

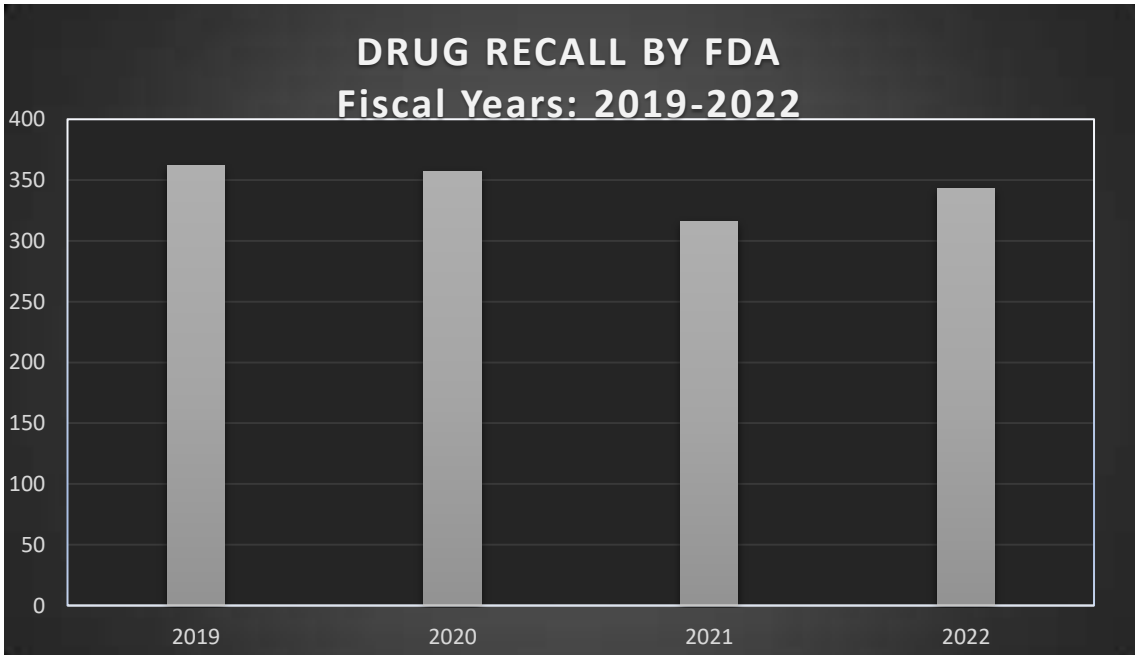


Figure 1: Drug Recalls by FDA (2019-2022)

Source: USFDA

The number of drug recalls by US FDA has been hovering around the 350 mark in the last four years. Countries around the world have to ensure more stringent regulations to reduce the number of recalls and avoid any untoward incidents.

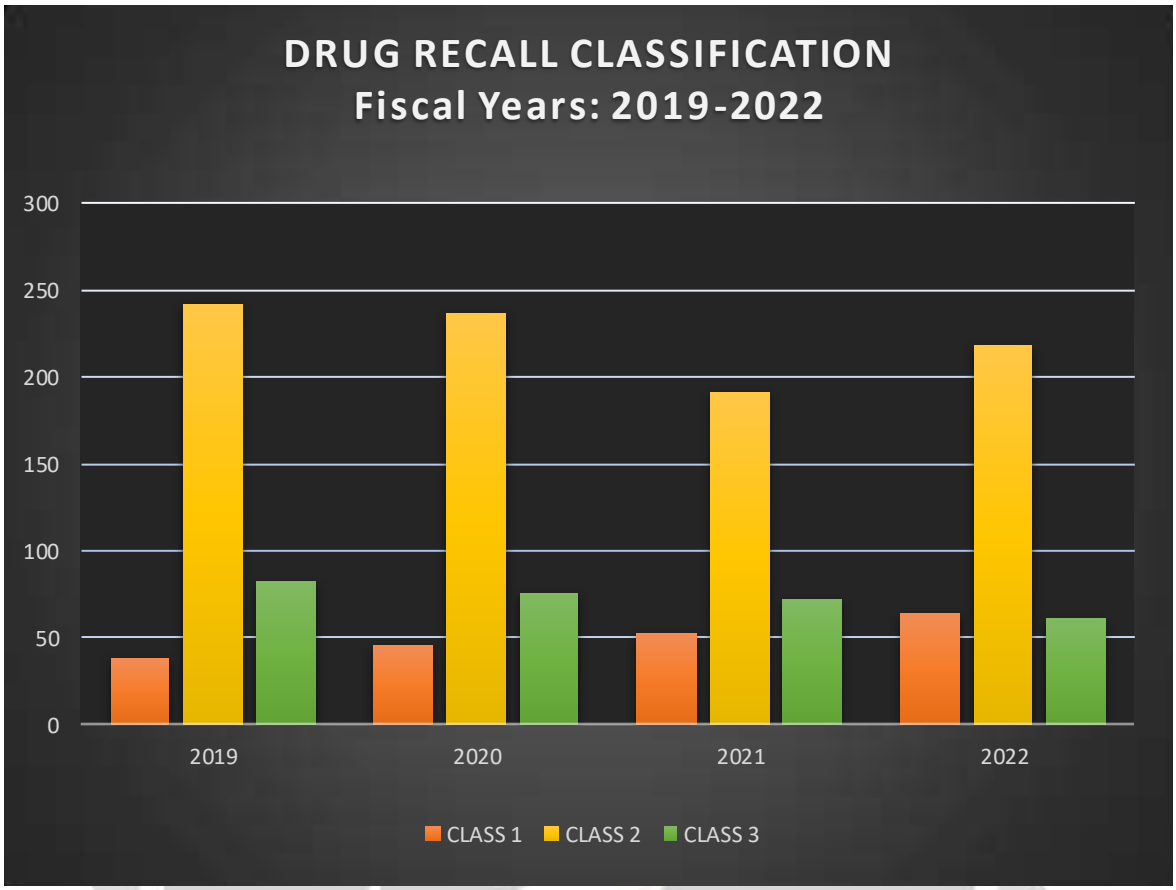


Figure 2: Drug Recall Classification (2019-2022)

Source: USFDA

Class 2 drug recalls have been more than any other recalls in the last couple of years as shown in graph above. Companies can have a special focus on class 2 drugs so that the right quality products are produced.

DRUG TESTING FACILITIES MUST BE INCREASED

One of the main suggestions is the requirement for state and federal drug testing facilities to be improved. Testing drugs requires a suitable infrastructure. There are drug testing facilities in only 15 states in India, and only seven of those are professionally manned and equipped. Institutions may be formed in conjunction with the regulatory body as centres for quality testing. The National Bioavailability Centre (NBC) at the NIPER, Mohali, and the centre at Jamia Hamdard, New Delhi, are two examples of institutions that can start up bioequivalence testing facilities. The majority of the research conducted at Jamia Hamdard's Pharmaceutical Medicine program are centered on bioavailability and bioequivalence studies in healthy volunteers. The centre at NIPER is accredited by the WHO and is one of the two centres in the world recognised for conducting bioequivalence studies of antitubercular drugs in fixed-dose combinations **(Khan & Ghilzai, 2007).**

The Central Drugs Standards Control is responsible for carrying out the control in India.State Drugs Control Departments (SDCD) under each State Government and the Central
Government's Drug Control Standard Operating sections of the Rules for the 1940 Drugs and Cosmetics Act. Due to the simultaneous construction of drug regulation process in India, the system has been crippled and is unable to provide patients with high-quality medications due to the limitations and overlapping functions of system. Drugs and Cosmetics Act, 1940 and Rules, 1945 provisions date from the time before independence and

didn’t have a thorough examination. Only a couple of changes based on requirement have been done and put into place.

DRAWBACKS

- **Lack of enforcement**: India's regulatory agency lacks the personnel and funding necessary to properly impose drug laws. The market is now flooded with subpar and fake medications as a result of this.
- **Corruption**: The Indian pharmaceutical business has been rife with it, and authorities have been charged of taking bribes to ignore breaches.
- **Inadequate testing**: India's regulatory system depends on producers to carry out their own testing, which could not be thorough enough to uncover all potential concerns.
- **Delays in approvals**: The bureaucratic and frequently long approval process for new drugs in India causes delays in patients' access to life-saving medications.

CORRECTIVE ACTIONS

- Increasing budget and staffing is necessary to ensure that regulations are effectively enforced by regulatory authorities
- Streamline the drug approval procedure: In order to ensure that patients receive life-saving medications as soon as possible, the drug approval procedure needs to be simplified.
- The regulatory system needs to be more transparent, with clear rules and regulations that the general people may easily access.
- Increase testing: To make sure that pharmaceuticals are both safe and effective, regulatory organisations must test them more frequently both before and after authorisation.
- Increased penalties for violations: To stop businesses from engaging in unlawful activity, the penalty for breaking drug regulations must be increased.
- Collaboration should be increased between regulatory bodies and nations. **(Rajesh et al., 2022)**

NEED FOR ARTIFICIAL INTELLIGENCE , MACHINE LEARNING AND BLOCKCHAIN TECHNOLOGY TO DECREASE DRUG RELATED INCIDENTS

All pharmaceutical firms are attempting to increase the effectiveness of their company procedures in order to research and develop new medications, to adhere to the industry's tight laws, and achieve the necessary results **(Kulkov I,2021).**

Researchers believe that the pharmaceutical industry will continue to develop as a result of big data and artificial intelligence algorithms. However, pharmaceutical firms must currently modify their approach and take advantage of new technological opportunities.

Such AI technology must first be tested alongside the existing technology it seeks to augment or replace, and the extra value must be presented and benchmarked in a way that is understandable, ethical, repeatable, and scalable - not only to users but also to regulatory bodies. Several pharmaceutical and artificial intelligence businesses have begun to collaboratively investigate this avenue **(Harrer S, 2019).**

Because of its versatility, pharmaceutical 3DP presents a plethora of alternatives during formulation creation that necessitate expert guidance. Using AI in Pharmaceutical With 3D printing, no human skill is necessary. because machine learning can reliably predict optimal process parameters.

Additionally, AI can be incorporated into a pharma 3 D printing 'Internet of Things,' turning the production of customized medications into an smart, effective, and self-sufficient pipeline. It will be crucial to have infrastructure, like the cloud and blockchain. Above all, these innovations will hasten the adoption of 3D printing for pharmaceuticals in clinical settings, accelerating the global transition to individualized medicine and Industry 4.0 **(Gupta R, 2021).**

The "Industry 4.0" refers to the fourth industrial revolution, which integrates quickly developing technologies like the IoT, AI, robotics, and advanced computing to fundamentally transform the landscape of production. Industry 4.0 is characterized by autonomous, self-contained, and integrated production systems. It will take innovative thinking to achieve Industry 4.0 for medications and get through the current nature of the present industrial infrastructure, regulation, and operations, **(Arden NS, 2021).**

Patients, doctors, hospitals/clinics, researchers, insurance payers, and pharmaceutical firms are just a few of the many distinct stakeholders in the complicated field of healthcare, all of whom rely heavily on patient data. The industry is becoming more digitalized, which may present potential for expansion in fields like tailored medicine, better health services, and better care
(Bublitz FM, 2019).

METHODOLOGY

The literature search was conducted on google scholar and pubmed, restricted to articles published from 2010-2023 as well as as google, USFDA website and news media like Reuters, Economic Times etc.The articles were searched online using the search words “drug related issues, contamination of drug, drug recall, digital transformation, drug incidents, drug tragedies” in research databases at Elsevier, TIPS, Researchgate, Springer.

Method of Analysis

Preferred Reporting Item for Systemic Reviews and Meta analytic (PRISMA) method was the method chosen to filter the required articles. Articles that fulfilled the selection criteria were then reviewed and summarised accordingly. The articles were screened for discrepancies in aim, publication year, the number of citations and recommendations for future investigations.

The articles that fulfilled the inclusion criteria were selected for the study. The included articles were cross checked to ensure that there are no duplicates and the information present in them was authentic and unique.

Criteria for Inclusion & Exclusion of articles

These included in current study, studies have to meet some criteria

(a) Studies have included some kind of selection criteria (drug related issues, recall procedures, drug contamination etc). These criteria limited the number of studies

(b) Accordingly excluded the studies in which it based on irrelevant information there is no proper Title, Abstract & Review.

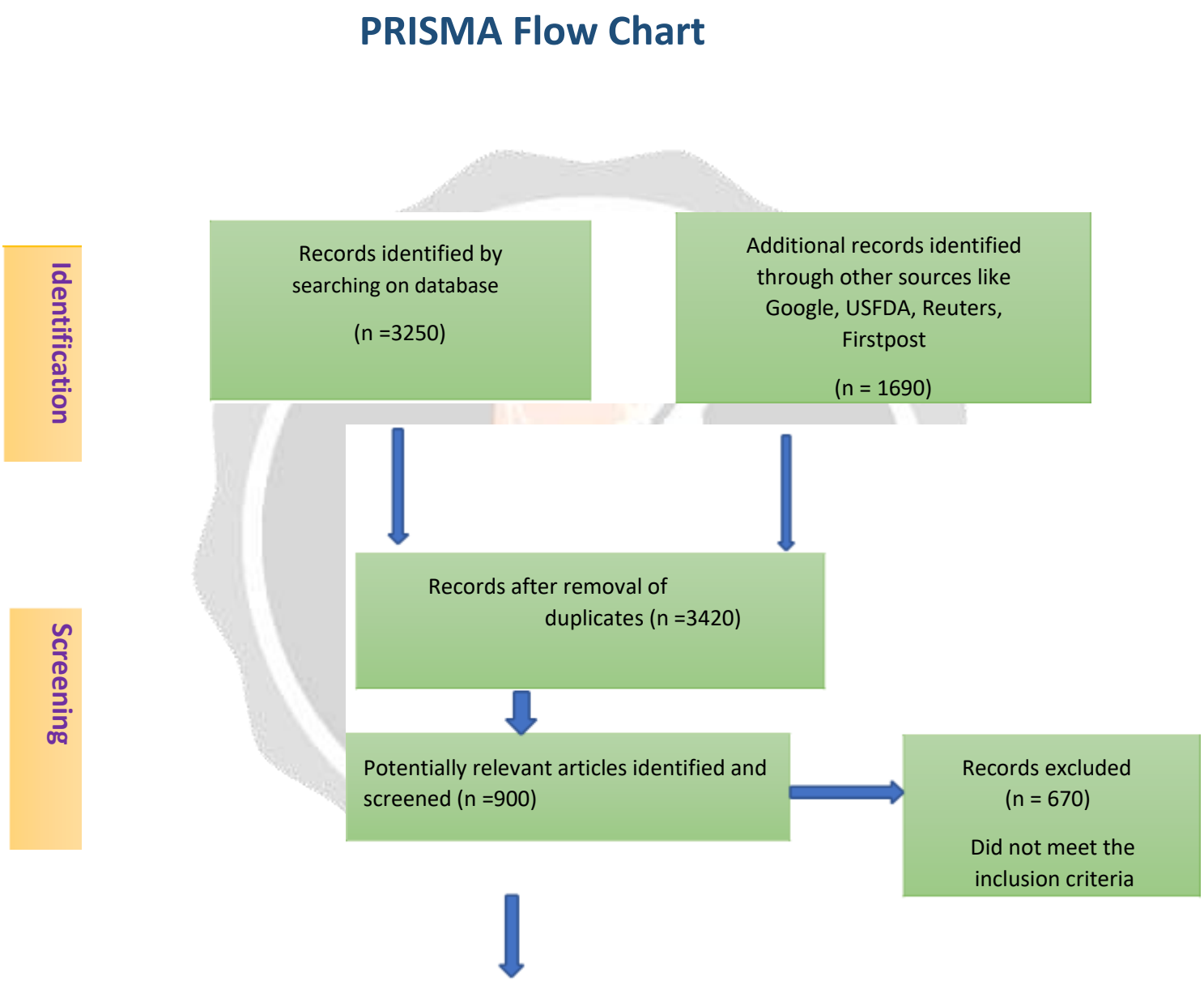
(c)Studies with duplicates of information with minute change between them or those that didn’t have proper citations were not included.

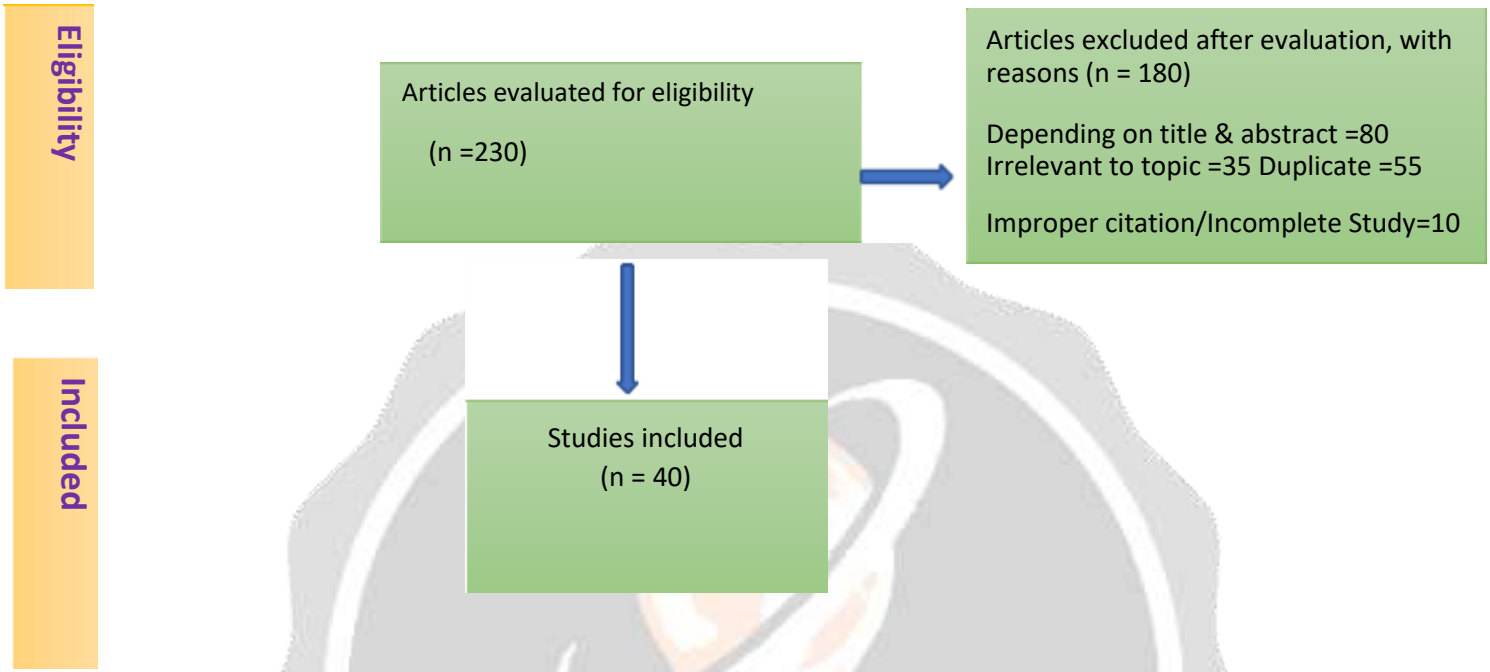
Final data set

The search on various research database like google scholar and pubmed using various keywords in search obtained 3250 research articles and 1690 from other sources. After checking the title, it was found there were many articles present in two different databases. The results after removing the duplicates were 3420 articles. A combined total

of 900 articles were screened. 670 articles were taken out from the study that they did not meet the inclusion criteria. Articles accessed for eligibility are 230 articles.

A Total number of 180 articles were excluded based on title and abstract (80) Irrelevant to topic (35), duplicate (55), incomplete study/ improper citations (10). The final data set consisted of 40 articles. The oldest included study was published in the year 2010 and the most recent study was conducted on 2023. The entire process is shown in figure below.




Eligibility
Articles evaluated for eligibility
(n =230)
Articles excluded after evaluation, with reasons (n = 180)
Depending on title & abstract =80
Irrelevant to topic =35 Duplicate =55
Improper citation/Incomplete Study=10
Included
Studies included
(n = 40)

DISCUSSION

Drug-related problems such as recall and contamination can be avoided through various measures, including strict regulations and quality control, monitoring and surveillance, education and training programs can help healthcare providers and patients recognize and respond to drug-related problems, collaboration among stakeholders, including government agencies, healthcare providers, drug manufacturers, and patient advocacy groups, can help identify and address drug-related problems. It's also clear that class 2 drug recalls have been higher in number in the last few years and companies have to focus on drugs belonging to these classes causing moderate toxicity. Incidents like cough syrup deaths in Gambia, Uzbekistan, illness caused by made in India cough syrup in West Pacific has tarnished the image of India as global pharma exporter. WHO is increasing alerts and Indian made drugs are coming under excessive scrutiny from the countries. Stricter regulations will help avoid such issue along embracing newer trends that help Indian Pharma boom worldwide.

CONCLUSION

Drug related issues have been a common occurrence in India every year. India, of late has had a lot of problems with cough syrups. India with its dual standard policy of exports has come under scrutiny from many countries. There is hence a need to make the guidelines more stricter so that drug recall and drug related issue can be avoided. This will improve the image of India as a global pharma exporter. The article dealt with many issues that developing countries like India is facing in its mission to be global pharmacy of the world. While, supplying in good quantity is important but equally important is quality. Developed nations can lend out their expertise and collaborate withy developing nations to help them produce the best quality of medicines and provide technologies that will streamline the supply chain process. As world is moving towards digital transformation, India too needs to embrace pharma 4.0 and use AI, ML and blockchain to run the manufacturing process efficiently and smoothly and deliver best quality medicines to the world.

REFERENCES

1. Milan Sharma (October 2022) Maiden Pharmaceuticals: WHO-flagged firm defaulted many times in various states for producing substandard medicines; *business today* retrieved from https://businesstoday.in

2. WHO (2022): Medical Product Alert N°6/2022: Substandard (contaminated) paediatric medicines, retrieved from https://www.who.int

3. Shrimansi Kaushik (Dec,2022) Maiden Pharma Cough Syrups That Killed 66 Gambian Children Are Of 'Standard Quality', Clarifies Centre *India news* ,retrieved from https://www.india.com

4. Bhartesh Singh Thakur (Feb, 2022): Maiden Pharma convicted in substandard ranitidine case *The Tribune,* retrieved from https://www.tribuneindia.com

5. Ashima shardha Mahindra (2023): Life-threatening bacteria found in Hyderabad company's cancer drug: WHO; *Times Now India*, retrieved from https://www.timesownews.com

6. *The news minute* (2023): Cancer drug produced by Hyderabad firm found contaminated in Lebanon and Yemen retrieved from https://www.thenewsminute.com

7. Health master (2022): Pharmacompany fined for dumping medical waste in open retrieved from http://thehealthmaster,com

8. Ambika Sharma (2022): Stop making anaesthetic that killed 5, Himachal Pradesh firm told, *the tribune* retrieved from https://www.tribuneindia.com

9. *Hindustan times* (2022): Propofol drug incident: PGI's internal panel submits report retrieved from https://www.hinsustantimes.com

10. *The Firstpost (*2022) Marion Biotech: The Noida-based pharma company at the centre of the Uzbekistan cough syrup tragedy Retrieved from https://www.firstpost.com

11. Ritesh K Srivastava (2023) 'Don't use cough syrups made by Noida-based firm Marion Biotech': WHO issues ALERT after Uzbekistan deaths *ZEE News* Retrieved from https://zeenews.india.com

12. *The BBC (2023)* Marion Biotech: India cancels licence of drug maker linked to child deaths in Uzbekistan Retrieved from https://www.bbc.com

13. Akriti Anand (2023) WHO warning: Don't use Marion Biotech cough syrups, linked to 19 deaths in Uzbekistan, for children Retrieved from https://www.cnbctv18.com

14. *Telegraph India* (2023) Contaminated cough syrup made in India found in Western Pacific: WHO Retrieved from https://www.telegraphindia.com/

15. Anwesha Madhukalya (2023) WHO says contaminated cough syrup made in Punjab found in Marshall Islands, Micronesia Retrieved from https://www.msn.com

16. *The Hindustan Times* India-made contaminated cough syrup found in Western Pacific nations, says WHO Retrieved from https://www.hindustantimes.com

17. *The Print* Contaminated cough syrup made in India found in Western Pacific countries, says WHO Retrieved from https://www.theprint.in

18. By Abinaya V(2023)WHO says contaminated cough syrup made in India found in Western Pacific *Reuters* Retrieved from https://www.reuters.com

19. Sundaran, S., Sankar, S., Dhamodaran, P., & Saji, S. M. (n.d.). *Drug Recall: an Overview*. *2*(2), 297–307. www.wjpr.net

20. Burrows VK. The FDA ' s Authority to Recall Products. 2010;

21. Fda.gov, (2020) All Ranitidine Products (Zantac): Press Release - FDA Requests Removal https://www.fda.gov.com

22. U.S. Food and Drug Administration. (2021, July 19). FDA Updates and Press

Announcements on NDMA in Metformin. Retrieved from https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-ndma-metformin

23. Business standard, (2023) Abbott recalls a batch of thyroid disorder drug for labelling error https://www.business-standard.com

24. Healthline (2019) Expanded Infant Ibuprofen Recall: Here's What You Should Know https://www.healthline.com

25. Kulkov I. Technology in Society The role of artificial intelligence in business transformation : A case of pharmaceutical companies. Technol Soc [Internet].

2021;66(May):101629. Available from: https://doi.org/10.1016/j.techsoc.2021.101629

26. https://www.telegraphindia.com/business/sun-pharma-hetero-recall-drugs-in-united-states-of-america-market/cid/1931742

27. https://brandequity.economictimes.indiatimes.com/news/marketing/sun-pharma-hetero-recall-drugs-in-the-us-market/99720405

28. Advance PA. Artificial Intelligence and Patient-centric Approaches to Advance Pharmaceutical Innovation. Clin Ther [Internet]. 2019;41(8):1406–7. Available from: https://doi.org/10.1016/j.clinthera.2019.06.014

29. Harrer S, Shah P, Antony B, Hu J. Arti fi cial Intelligence for Clinical Trial Design. 2019;40(8):577–91.

30. Gupta R, Srivastava D, Sahu M, Tiwari S, Ambasta RK, Kumar P. Artificial intelligence to deep learning : machine intelligence approach for drug discovery

[Internet]. Vol. 25, Molecular Diversity. Springer International Publishing; 2021. 1315–1360 p. Available from: https://doi.org/10.1007/s11030-021-10217-3

31. Arden NS, Fisher AC, Tyner K, Yu LX, Lee SL, Kopcha M. Industry 4 . 0 for pharmaceutical manufacturing : Preparing for the smart factories of the future. Int J

Pharm [Internet]. 2021;602:120

32. 1.Centers for Disease Control and Prevention. (2021). Overdose Deaths. Retrieved from https://www.cdc.gov/drugoverdose/data/index.html

33. 2.American Medical Association. (2021). Issue Brief: Reports of Increased Overdose and Other Concerns during COVID-19 Pandemic. Retrieved from https://www.ama-assn.org/system/files/2021-03/issue-brief-increased-overdose-other-concerns-covid-19-pandemic.pdf

34. 3.Nichols, D. E. (2016). Psychedelics. Pharmacological Reviews, 68(2), 264–355. https://doi.org/10.1124/pr.115.011478

35. 4. Food and Drug Administration. (2018). FDA updates recalled valsartan-containing product information. Retrieved from https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-recalled-valsartan-containing-product-information

36. 5.US Food and Drug Administration. (2019). FDA announces voluntary recall of several medicines containing valsartan following detection of an impurity. Retrieved

from https://www.fda.gov/news-events/press-announcements/fda-announces-voluntary-recall-several-medicines-containing-valsartan-following-detection-impurity

37. US Food and Drug Administration. (2020). FDA updates on hand sanitizers consumers should not use. Retrieved from https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-hand-sanitizers-consumers-should-not-use

38. Johnston, A., & Holt, D. W. (2014). Substandard drugs: A potential crisis for public

health. *British Journal of Clinical Pharmacology*, *78*(2). https://doi.org/10.1111/bcp.12298

39. Khan, A., & Ghilzai, N. (2007). Counterfeit and substandard quality of drugs: The need for an effective and stringent regulatory control in India and other developing countries. *Indian Journal of Pharmacology*, *39*(4). https://doi.org/10.4103/0253-7613.36541

40. Rajesh, S., Dhamotharan, J., Kumar, P. S., Babu, M. A., Jagadeesan, M., & Reddy, K. T. K. (2022). Eradication of spurious adulterated and under standard quality drugs, a regulatory pertaining in Indian regulatory system. *International Journal of Health Sciences*. https://doi.org/10.53730/ijhs.