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## Analytical Incidents In the Pharmaceutical Industry: A Review

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### ABSTRACT

Incidents are Analytical Incidents that occur during analytical testing that affect the quality of the product. This paper includes a study to ensure the quality and safety of drugs and also avoid future incidents. The research is based on the root cause of incidents and their patterns. To overcome these incidents, quality audits are performed. These incidents are important for the following reasons. Product quality: Analytical incidents can impact the quality of pharmaceutical products, which can affect patient safety and efficacy. Patient safety: Inaccurate or unreliable analytical results can lead to incorrect labelling, potency, or purity of pharmaceutical products, which can harm patients. It Ensures compliance with regulatory requirements, such as FDA, EMA, and ICH guidelines. Prevents regulatory actions, fines, or penalties. These incidents prevent financial losses due to retesting, rework, and product recalls. It prevents damage to a company's reputation and brand.&. Maintains customer trust and confidence. The recent research is mainly focused on methods and corrective action used for accuracy, reliability, and consistency of analytical testing. The recent themes are Data Integrity and security, which are used for maintaining digital records in the laboratory. It also includes continuous improvement and digitization, which are emerging new technologies. The main point of this article is to analyse the root cause of Incidents and corrective action taken on these analytical incidents. This topic is interesting because it brings together ethical and technological challenges that affect human health. These analytical incidents investigate the whole process of the pharmaceutical industry.

**Keywords:** Analytical incidents, root cause, Good Manufacturing Practices, Analytical testing, strengths, fishbone diagram

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## INTRODUCTION

Analytical incidents occur in India about 38%. The various reasons like equipment quality, human error, software etc. The pharmaceutical industry has performed Quality audits to prevent this kind of incidents. To avoid future incidents and ensure safety, efficacy, quality of product identification and investigation is also important. Analytical incidents occur at any stage during the manufacturing of drugs like formulation, packaging, storage etc. The analytical incidents cause financial loss to the pharmaceutical industry. Nowadays, cyber-attacks on the pharmaceutical industry are increasing. There are also other types of analytical incidents and they are related to humans (Analysts), chemicals, Instruments etc. There are various pharmaceutical companies that commit fraud in analytical testing. There are many methods developed and developed for investigating analytical incidents. The importance of this paper is to avoid future analytical incidents and distribute information all over the world.

### SCOPE:

The scope of incidents involves the following points:

#### Reporting the incident to the QA head:

All information regarding incidents is given to the QA head. e.g. incident related to chemical or software or cyber-attack.

#### Evaluation:

The incident is evaluated and any recommendations or remedies for the incident are taken through experts and heads.

#### Corrective action was taken on the incident:

Corrective action is taken on analytical incidents. For e.g., If a human human-related incident occurs then it is corrected by humans.

#### Close the incident:

The quality assurance head closes the incident and fills in compliance details.

#### Incident number:

Product name	Batch No.	Name of analyst	Observation	Action taken	Submit

Date:

Test to be performed:

## CLASSIFICATION OF INCIDENTS:

Human related incidents

Chemical related incidents

Instrument related incidents

Cyber attack

### **Human [Analyst] related incident:**

In this, incidents occur due to analysts. This occurs because of poor skill, wrong decisions, poor leadership, insufficient knowledge, miscommunication between workers etc. These all things are responsible for such kind of incidents.

This type of incident can be avoided by including the following points:

- Great leadership
- The person should know the guidelines of GLP, GMP
- Good communication between worker

### **Chemical-related incidents:**

These incidents occur due to chemicals used in the pharmaceutical industry. The chemicals used for testing or any other process should be taken from an authorized vendor.

- The chemicals used must be pure and non-hazardous.
- These types of incidents occur because of improper handling of drug
- For ex. The impure chemicals can cause these types of incidents and cytotoxic drugs are handled properly

### **Instrument-related incidents:**

This type of incident occurs due to an instrument. This occurs because of improper working of instruments, changes in instruments, use of different types of instruments for the same process, improper cleaning of equipment etc.

These incidents can be avoided by following points:

Calibration of instrument

Quality audits are performed

Cleaning of instrument

### **Cyber Attacks:**

Nowadays, this problem is increasing. the cyber-attack can cause loss of confidential information, files, data, and important documents. There are many cyber-attacks that occur in various pharmaceutical industries. E.g. the cyber-attack is on Sun pharmaceutical industries in 2023. In this ALPHV group does a ransom ware attack on Sun Pharma to steal important data and

documents. The Sun Pharma company isolated the network, initiated recovery procedures and called cyber security experts.

- There are other examples of cyber-attacks on the pharmaceutical industry like Dr. Reddy's laboratories
- To avoid such types of incidents employee awareness programs should be performed and also training programs.
- Nowadays we can use AI to prevent such incidents. In this machine learning is important.
- This type of incident may cause financial loss to the pharmaceutical industry.

## MATERIALS AND METHOD

### Contents:

Good Manufacturing Practices [GMP]: A set of guidelines enforced by regulatory agencies (e.g., FDA, EMA) that outline the standards for ensuring quality in pharmaceutical manufacturing. GMP guidelines play a critical role in preventing analytical incidents.

The FDA's 21 CFR 211(GMP regulations) provide specific requirements for testing, validation, and documentation of analytical results in pharmaceutical manufacturing

Good Laboratory Practices [GMP]: These Guidelines are for laboratory practices, for example. OECD Principles of GLP provide a framework for testing and maintaining quality assurance in laboratory settings.

International Council on Harmonization [ICH Guidelines]: The ICH provides harmonized guidelines for drug development, including methods for analytical testing and validation for example, ICH Q2 [R1] Guideline for analytical methods

### METHODS:

- Root cause analysis (RCA)
- Fishbone diagram
- SWOT analysis
- Five whys method
- Failure modes and effect analysis (FMEA)

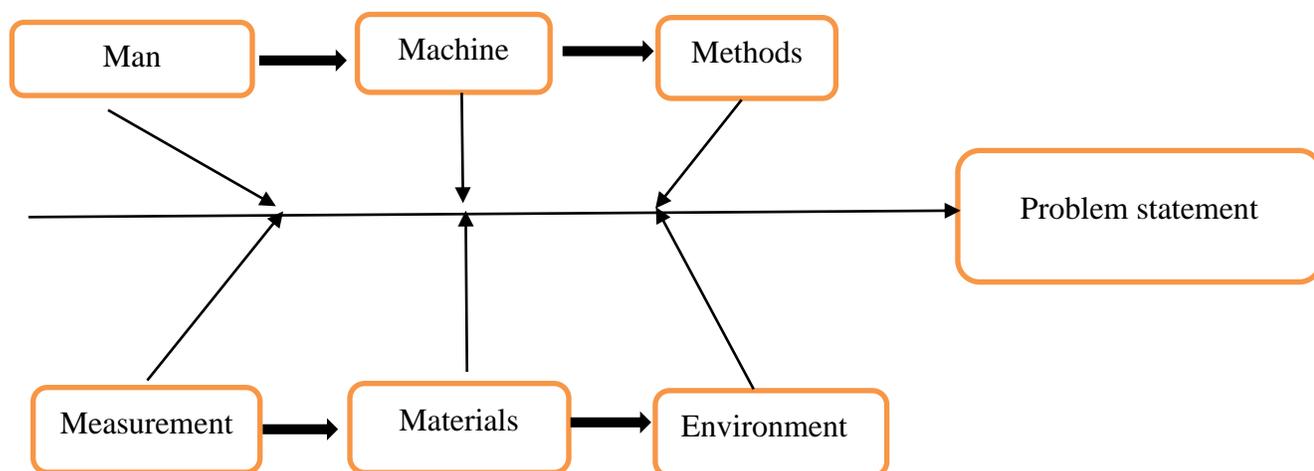
### Root causes Analysis:

Root cause analysis is an effective method to achieve this particular goal. Root cause analysis is a technique to achieve a non- conformance to find out the real cause of particular problem. For investigation, various root cause analysis tools are used. The main aim of root cause analysis is the actual cause of an observed problem, defect, or failure so as to used for this particular information to correct it. After the investigation and identification of appropriate root cause the implementation

of CAPA (Corrective Action and Preventive Action) should be done. Suppose any specific pharmaceutical company which provide drug products and healthcare products to customer. The company expand its global presence but their product stock outs are increased with Increasing business. The pharmaceutical company identify that quality defects in manufacturing and production process and there will be difficulty to meet customers demand to address the challenge company research on product- stock outs.

### Fishbone Diagram:

Fishbone diagram is representation to identify cause of analytical incidents. It is look like fish skeleton . The problem is placed on head and mouth of fish and other causes of problem is on smaller bone of fish .The diagram include causes of incidents. Fishbone diagram gives practical cause to audience [manufacturing team] think that practical cause in brainstorming session . In brainstorming session all team members are present . In this session, all of team members are give idea about potential causes regarding incidents this is placed on smaller bone of fish and it and also include process, man, material, method



**Figure 1: Fishbone Diagram**

### SWOT Analysis:

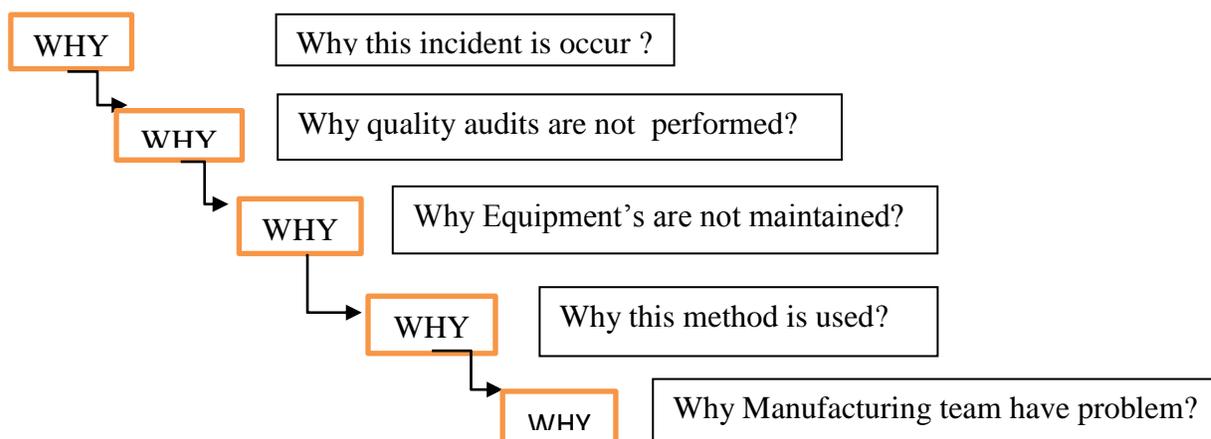
This analysis, which is used for Strengths, Weaknesses, Opportunities, and Threats, helps in understanding both internal and external factors that can impact your business. Strengths and weaknesses are internal to the business, while opportunities and threats are external

In this company identify strengths **like** high demand of medicines, strong research and development process, regulatory approval of new drugs etc.

It evaluates weakness regarding R&D because it is very expensive process, patent expiry, long time process like approval of new drugs etc.

The industry catches opportunities like growing markets in India, China, Brazil etc, the aging population, innovation of biotechnological medicines, use of artificial intelligence in pharmaceutical industry, use of gene therapy.

It also working on threats like increasing use of generic medicines, pollution affects the manufacturing process, affects public health [adverse effects], pricing pressure



**Figure 2: Five Why's Method**

**Five why's Method:** In this method ask 'why's multiple methods for analysis of root cause

#### Benefits

1. We Obtain record for future incidents
2. We obtain detail information about given incident.

#### Drawback

1. This method is not suitable for complex problems.
2. This method only analyze single root cause.

#### Failure modes and effect analysis (FMEA) :

FMEA is systematic method in which risks of product and process are analyzed. It supports GMP [Good Manufacturing Practices]

Types of FMEA

Service FMEA

Process FMEA

Design FMEA

System FMEA

**Service FMEA:** in this drug product is checked before reaching the customer. It involves method, procedure, workers for material handling. To analyze root cause it should be performed multiple times.

**Process FMEA:** During this manufacturing process is checked. It involves product, machines, process is checked. It should identify the defects in the process. It analyze the risk during production phase. It also determines the weak point of system like machine, method, process etc.

**Design FMEA:** Design FMEA is used before starting production. It examines product failures that will occur because of failures in the design at the manufacturing stage. In short, the determination of all the failures that may arise in the design and properly defined.

**System FMEA:** During the design phase system and sub-systems analysis, FMEA is used for determining the type of failure resulting from system deficiencies.

RPN Number: Risk priority number (RPN) is a value obtained by multiplying occurrence, severity and detection values as Eq. (1). Risk Priority Number (RPN) =Occurrence (O) x Severity (S) x Detection (D) . RPN is defined and calculated for failures. After this calculation the failures are ranked from small to large due to RPN values

#### RESULTS AND DISCUSSION:

Results: Analytical incidents related to Instrument can affect drug quality, safety, and efficacy. These impure drugs reached to market can affect public health. If such incidents detected in clinical trial there will be delay in further process. These incidents can cause violation of Good Manufacturing Practices [GMP] this may cause suspension of manufacturing process of given company. In extreme cases, if analytical issues point to systemic problems or fraud, regulatory agencies may revoke a product's approval or even a company's license to operate in certain markets. This type of incidents lead to legal action taken by consumers, healthcare providers, customers and loss of consumer's trust. This also affects drug brand value. These type of incidents affect on stock price of given pharmaceutical company. Pharmaceutical companies could face the loss of intellectual property or patent rights. This could make the drug more used for competition or generic use analytical incidents in the pharmaceutical industry can have profound consequences, affecting product safety, regulatory standing, financial performance, public health, and a company's reputation. Proactively managing risks through stringent quality control, compliance, and transparent processes is essential to minimizing the impact of such incidents.

After the analytical incident occurs in pharmaceutical company it try to avoid such type of cases. The company implement some strategies. The company can apply strategy like continuous training of employee. In these all employee are trained by Good Manufacturing Practices & 21 CFR. The staff also trained by new technologies regarding drug manufacturing process. The Quality audits are performed by third party. Developing and maintaining a detailed crisis

management strategy to handle analytical incidents swiftly, including communications with regulators, customers, and the public. The all Equipment are used in pharmaceutical company that are calibrated and qualified.

Discussion: The discussion is regarding causes, types, consequences, and solutions associated with analytical incidents, as well as their effect on the pharmaceutical industry. The analytical method is used for testing of drugs should be validated because if not validated then false results are obtained for example the study designated for dissolution rate can produce false results due to out of calibration . the methods are used for minimize the analytical incidents that are also discussed . The new technologies are involved in discussion. Automation can reduce human error in analytical testing. Using automated systems for data collection, analysis, and reporting can improve accuracy and reproducibility while reducing the mistakes. Analytical incidents in the pharmaceutical industry are serious events that can have wide-ranging problem, from regulatory consequences to patient safety concerns and reputational damage. these issues requires a proactive approach that includes rigorous quality control, continuous training, and adherence to best practices. The pharmaceutical industry must remain vigilant and responsive to the potential risks associated with analytical incidents, as patient safety and product quality must always remain the highest priority.

#### CONCLUSION:

Pharmaceutical incidents, including analytical incidents, can have significant consequences on product quality, patient safety, and regulatory compliance. It is essential for pharmaceutical companies to have a robust system in place for identifying, reporting, investigating, and correcting incidents. It is used to establish a robust incident management system that includes procedures for reporting, investigating, and correcting incidents and provide regular training to personnel on incident reporting, investigation, and CAPA implementation .These Conduct regular audits and reviews of processes and systems to identify potential vulnerabilities and implement corrective actions. It is used to Foster a culture of transparency, accountability, and continuous improvement within the organization.

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