



Managing Deviations in Pharmaceutical Manufacturing: Case Studies and Regulatory Compliance

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ABSTRACT

This article delves into the intricacies of managing deviations in pharmaceutical manufacturing, emphasizing the critical role of adherence to regulatory standards and the implementation of effective quality control measures. It explores the various types and classifications of deviations, ranging from planned to unplanned and critical to minor, providing insights into their significance in maintaining product quality and safety. The article outlines a structured procedure for handling deviations, encompassing investigation processes, root cause analysis techniques, and closure strategies.

Furthermore, through real-world case studies of pharmaceutical companies facing deviation-related issues, the article highlights the consequences of non-compliance with regulatory guidelines. These case studies illustrate how deviations can impact product quality, safety, and regulatory standing, emphasizing the importance of stringent quality assurance practices.

Ultimately, the article underscores the imperative of proactive deviation management, risk assessment, and corrective actions, offering a comprehensive understanding of how pharmaceutical manufacturers can navigate the complex landscape of deviations to ensure product quality, regulatory compliance, and consumer safety.

1. INTRODUCTION

Deviations represent quantifiable disparities between observed values and the anticipated or standard values for a product or process condition, encompassing deviations from established guidelines or procedures. These deviations can manifest during the evaluation and sampling phases of both finished products and incoming raw materials, as well as within the manufacturing process itself. Additionally, customers' complaints and feedback may reveal deviations when a company's standards fail to align with the critical quality attributes specified in requirements. To uphold a commitment to continuous enhancement and adherence to Good Manufacturing Practice (GMP) standards, any instance of deviation from established protocols necessitates thorough documentation. This documentation mandate aligns with the Food and Drug Administration's (FDA) requirement, as specified in FDA part 211.192, which stipulates comprehensive investigation of any deviation, including the recording of findings and subsequent actions. Incorporating Quality Risk Management (QRM) principles within the organization ensures that all identified deviations are promptly addressed, rectified, and meticulously documented, fostering a culture of quality assurance and regulatory compliance.

2. TYPES OF DEVIATION: ^(2,3)

There are two primary categories of deviations: Planned deviations and Unplanned deviations.

2.1 Planned Deviations:

Planned deviations involve intentionally deviating from standard procedures for a short period. This is done to prevent undesirable situations without compromising the safety and quality of the product or process. An example of a planned deviation is when a batch is executed with lower inputs due to the temporary unavailability of raw materials.

2.2 Unplanned Deviations:

Unplanned deviations, on the other hand, are unintentional deviations from the established procedures that occur either during or after the execution of an activity. These deviations can arise due to various reasons such as equipment breakdown, power supply interruptions, site accidents, utility failures, or errors in documentation.

Deviations can be further categorized into three types based on their impact on product quality, safety, and the validation status of the facility and process:

2.2.1 Critical Deviation: :

A critical deviation has a significant impact on the critical attributes of the product. For example, using contaminated raw materials and solvents or experiencing an integrity failure of high-efficiency particulate air filters

2.2.2 Major Deviation:

A major deviation can potentially affect the critical attributes of the product. This includes critical process failures and deviations from the standard output range that are significant enough to be of concern.

2.2.3 Minor Deviation:

Minor deviations do not directly impact the quality of the product. Examples of minor deviations include not replacing weights properly after use or encountering equipment and measuring device malfunctions.

These categories help in assessing the severity of deviations and guide appropriate actions to address and document them in a systematic manner.

3. CLASSIFICATION OF DEVIATION:

To effectively document, categorize, and examine incidents according to their level of risk, a decision tree will be employed. This decision tree provides a straightforward risk assessment, addressing the inquiries outlined in **Figure 1**, enabling individuals to make informed decisions in response to these events.

3.1 Flowchart is as follows:

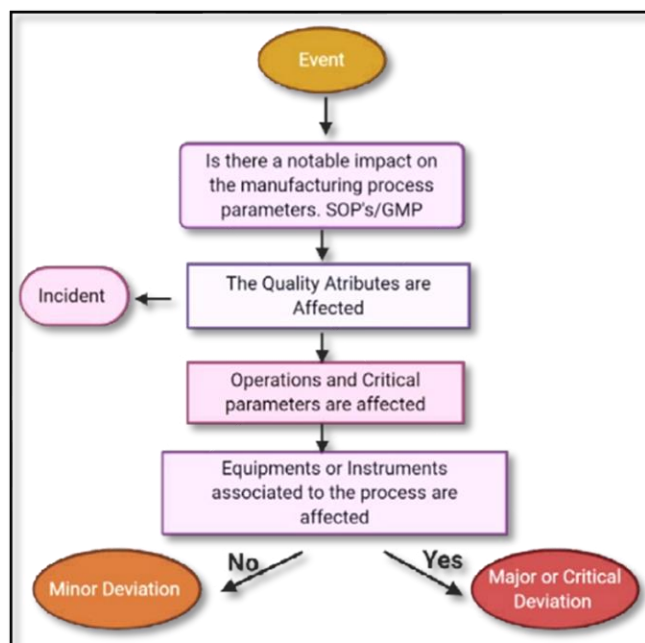


FIGURE:1 www.ijpsonline.com

4. PROCEDURE FOR DEVIATION HANDLING: (2,3,4)

4.1 How to deal with a deviation:

If something goes wrong, you should tell QA right away or follow the SOP. You have one day to report the deviation from when it happened.

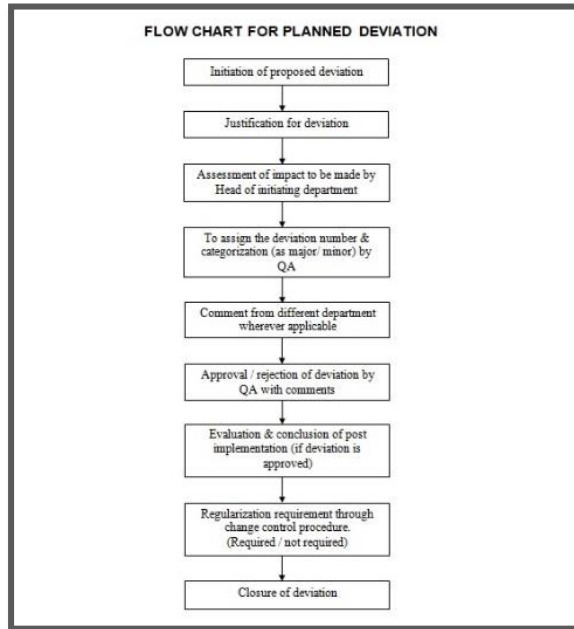


FIGURE:2 <https://www.pharmaguideline.com/2014/07/deviation-flowchart.html>.

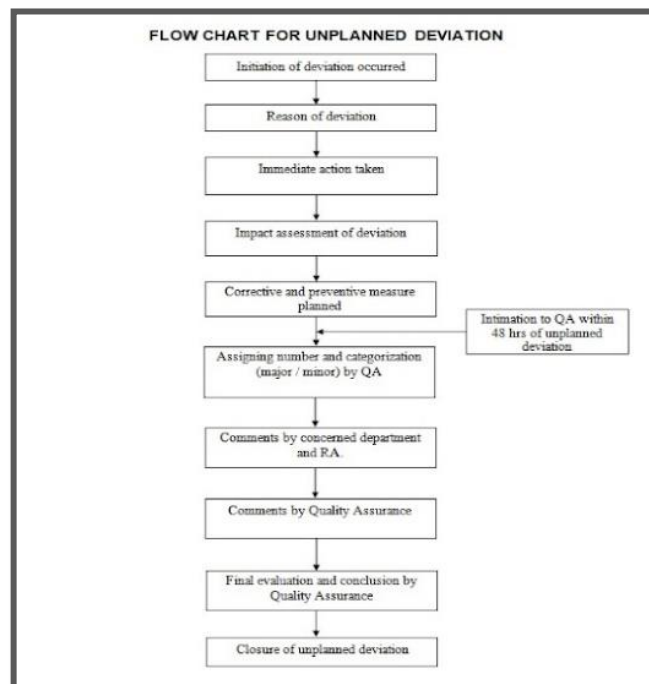


FIGURE:3 <https://www.pharmaguideline.com/2014/07/deviation-flowchart.html>.

4.2 INVESTIGATION PROCESS:

Steps in the investigation process:

1. Promptly notify the relevant user department as soon as a deviation is detected.

2. Conduct an initial analysis.
3. Assess all the presently accessible information.
4. Interview the relevant individuals.
5. Develop immediate measures or remedial actions based on the initial evaluation. Fundamental knowledge and practical familiarity with incidents and investigations: Fundamental understanding and practical expertise in handling incidents and conducting investigations. Familiarity with processes and the associated systems.
6. Inquiry process and gathering of data:
 - Examination of records and paperwork.
 - Review of similar incidents that occurred in the past five years.
 - Interviews with personnel involved in the history of product incidents.

4.3 ROOT CAUSE ANALYSIS

Root cause analysis is a methodical way of finding out the main reasons for problems or events and how to deal with them. Root cause analysis can be divided into five types of errors that are caused by People, Materials, Machines, Methods and Nature.

Some tools that can help find the root cause are:

4.4 Fishbone Analysis:

Fishbone Analysis, also known as the Ishikawa diagram, is a visual tool used to classify potential reasons for a deviation with the aim of pinpointing the underlying cause. This method, introduced by Japanese quality control expert Ishikawa, is employed to uncover the root cause behind unidentified deviations. It involves a comprehensive examination of various factors such as equipment, measurements, personnel, environment, methods, and materials to identify potential causes. When a deviation is related to a particular process, the various stages of that process are also incorporated into the fishbone analysis.

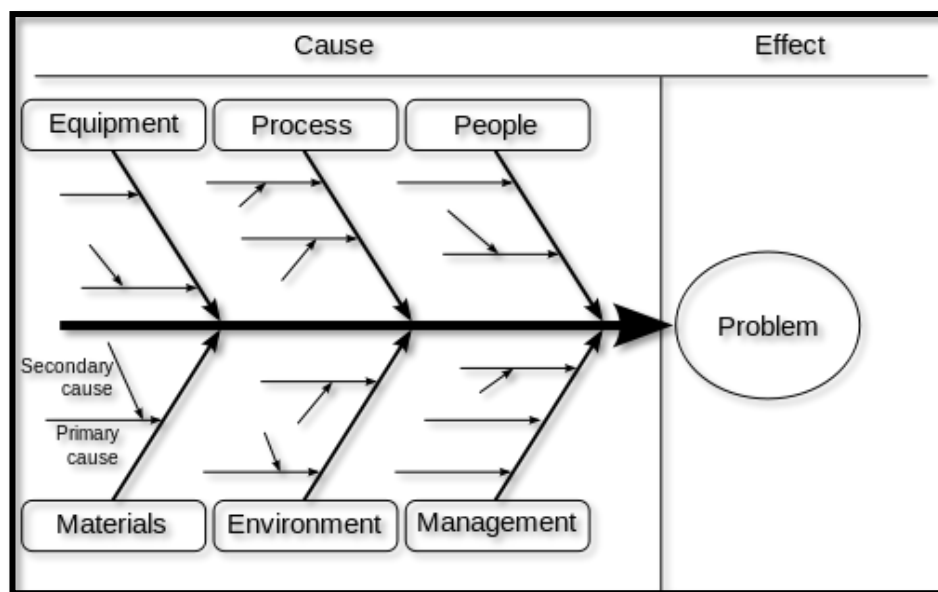


FIGURE:4 https://upload.wikimedia.org/wikipedia/commons/thumb/5/52/Ishikawa_Fishbone_Diagram.svg/500px-Ishikawa_Fishbone_Diagram.svg.png?20090408130103

4.5 FIVE WHY'S:

In order to pinpoint the underlying reason behind a deviation, the five why's technique should be employed in conjunction with the cause and effect diagram for a more in-depth exploration (as depicted in Figure 4). This analytical approach is likely to unveil the fundamental cause of non-compliance. The method is applied in the following steps:

1. Begin by determining the initial point where non-compliance needs further analysis.

2. Employ logical reasoning to identify the root cause prior to commencing any investigative activities.
3. For each identified cause, continually query the system, asking, "Why is this the cause of non-compliance?"
4. Repeat this questioning process iteratively until the root cause is uncovered.

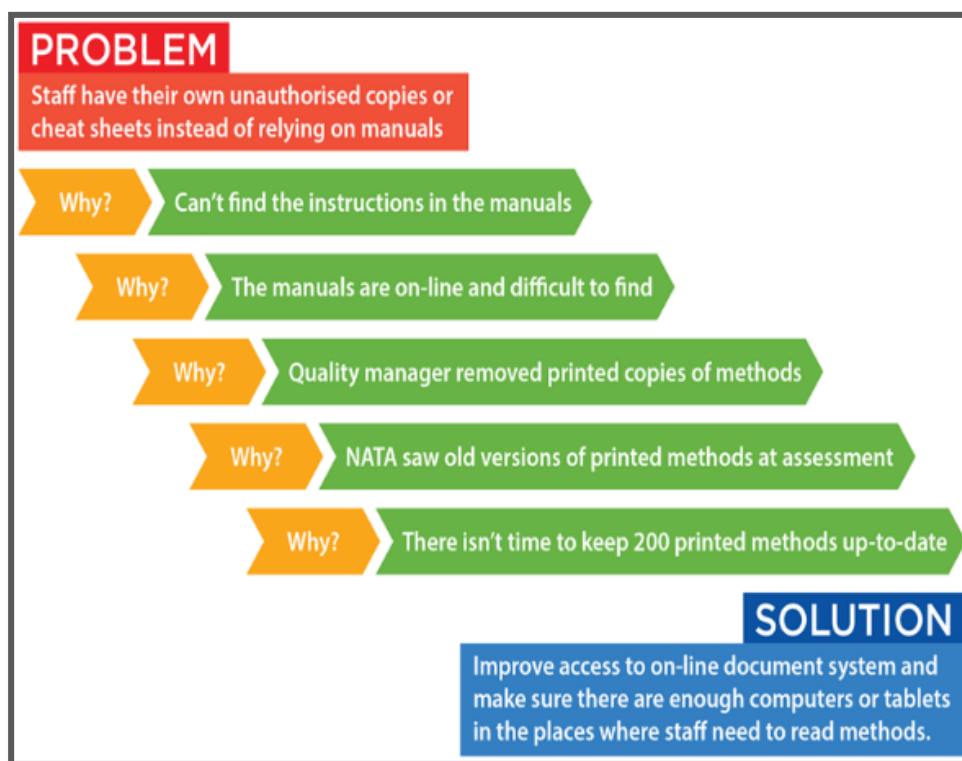


FIGURE:5 <https://www.linkedin.com/pulse/how-use-5-whys-analysis-identify-root>

4.6 5W and 1H Technique:

This technique is employed when dealing with instances of failure. The key steps to focus on are as follows:

1. What: Determine if all relevant information regarding the non-compliance has been gathered.
2. Who: Assess whether the operators involved in the activity possess the necessary training and experience..
3. When: Identify the timing of when the non-compliance occurred.
4. Where: Evaluate whether the location is appropriate for carrying out the process activities.
5. Why: Investigate the underlying reasons for the non-compliance.

Once the 5W questions have been addressed, the next step involves questioning the conclusion by asking "How?"

4.7 FAULT TREE ANALYSIS:

Fault tree analysis is a method used to identify the underlying causes of deviations. It enables the examination of system failures one step at a time, and occasionally, by recognizing the chain of events leading to the issue, multiple causes can be linked together.(2) Fault tree analysis is a tool employed for conducting root cause analysis of deviations. It assists in systematically assessing the breakdown of a system one element at a time, and on occasion, by pinpointing the sequential chain of events, it's possible to connect multiple causes.The outcomes of these events are visually represented in a tree-like structure. FTA is utilized for investigating deviations and complaints, with the goal of comprehending their root causes and implementing enhancements to prevent future issues from arising . Additionally, there are various other methods for identifying the causes, including Pareto charts, brainstorming, flowcharting, and change analysis .

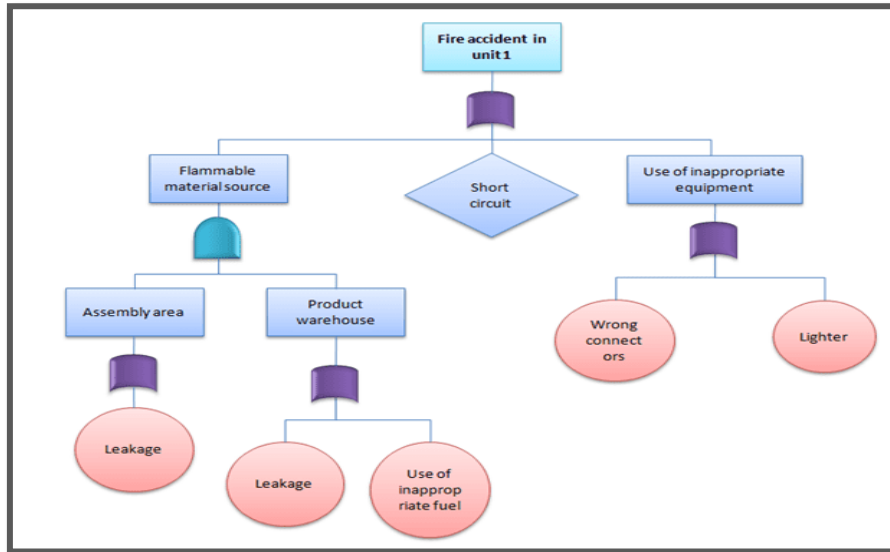


FIGURE:5 <https://sixsigmastudyguide.com/fault-tree-analysis/>

4.8 CLOSURE OF DEVIATION:

The Head of the QA department is tasked with resolving deviations following an investigation and CAPA proposal. This entails providing comprehensive information regarding the deviation, encompassing aspects such as its recurrence, deviation type (whether planned or unplanned), deviation category (whether critical, major, or minor), and whether a CAPA is recommended or not. If a CAPA is recommended, the CAPA number should be recorded. Moreover, any pertinent supporting documents must be enclosed, and the closure should be endorsed with the individual's name, signature, and date.

CASE STUDY: 1⁽⁵⁾

1.1 NAME OF COMPANY: GREEN PHARMACEUTICALS

1.2 ISSUE: The company's firm failed to conduct at least one test to verify the identity of each component of a drug product (21 CFR 211.84(d)(1)).

In simpler terms, you make over-the-counter drugs that people can buy without a prescription. The problem is that you didn't properly test some of the ingredients you used, especially those that could be contaminated with a harmful substance. This substance can be very dangerous if it gets into the drugs.

In the United States, there are rules for testing these ingredients to make sure they are safe. The company didn't do this testing, which means they couldn't be sure if these ingredients were safe to use in their drugs.

Using ingredients with contamination can be extremely dangerous and has caused people to get seriously sick or even die in different parts of the world.

1.3 IN RESPONSE PROVIDE THE FOLLOWING:

The FDA has a guide that can help the company follow the rules and make sure their drugs are safe when they use ingredients that could be contaminated.

1. Timely Testing of High-Risk Drug Components:

- The company must commit to providing test results for certain high-risk drug components within 30 days from the date of this letter.
- If they cannot provide retained samples of these components, they should perform testing on finished drug product batches to ensure there's no contamination.

2. Risk Assessment for Drug Products:

- The company must conduct a comprehensive risk assessment for drug products that might contain contaminants.
- Any products within their expiration date, containing ingredients at risk for contamination, should be thoroughly evaluated for safety.
- If contamination is found, the company should promptly take necessary actions, including customer notifications and product recalls.

3. Corrective and Preventive Actions (CAPA):

- The company should identify and implement corrective actions and preventive measures to ensure secure supply chains in the future.
- This might involve sourcing raw materials only from qualified manufacturers and ensuring they are free from unsafe impurities.
- Details of these actions must be provided in response to this letter.

4. Testing of Component Lots:

- The company needs to describe how they will test each component lot for conformity with specifications related to identity, strength, quality, and purity.
- If they plan to rely on supplier's Certificate of Analysis (COA), they must explain how they will validate and periodically revalidate the reliability of these results.
- Additionally, they must commit to conducting at least one specific identity test for each incoming component lot, including specific tests for certain high-risk components.

5. Chemical Quality Control Specifications:

- The company should provide information about the chemical quality control specifications they use to determine the acceptability of incoming lots of high-risk drug components for use in manufacturing.

6. Supplier Qualification and Material Control:

- There should be a thorough, independent review of the company's material system.
- This review should assess whether all suppliers of components, containers, and closures are qualified.
- Adequate controls should be in place to prevent the use of unsuitable components, containers, and closures.

1.4 Conclusion: This warning letter summarizes significant violations of Current Good Manufacturing Practice (CGMP) regulations for finished pharmaceuticals. In essence, this letter outlines the regulatory expectations for ensuring the safety, quality, and traceability of all materials used in drug manufacturing, especially high-risk components. The company is required to take a series of actions to comply with these standards and provide detailed responses regarding their processes and plans.

CASE STUDY: 2⁽⁶⁾**2.1 NAME OF COMPANY: LEX INC.****2.2 ISSUE: The company's firm's quality control unit failed to exercise its responsibility to ensure drug products manufactured are in compliance with CGMP, and meet established specifications for identity, strength, quality, and purity (21 CFR 211.22).**

In company's firm, there are significant issues with the quality system, particularly in relation to the oversight of over-the-counter (OTC) drug product manufacturing. The Quality Unit (QU) has failed to ensure various critical aspects, including:

1. **Lack of Clear Responsibilities:** There are no well-defined written procedures outlining the roles and responsibilities of the Quality Unit.
2. **Component and Product Approval:** The QU has not been effectively approving or rejecting all components and drug products, raising concerns about the quality control process.
3. **Inadequate Record Review:** There has been a failure to adequately review production and control records to ensure they are complete and error-free, which is essential for product quality.
4. **Impact Assessment:** The QU has not been involved in the approval or rejection of procedures or specifications that may affect the identity, strength, quality, and purity of drug products.

Furthermore, there is a lack of adequate control over the inspection and release of lots of components, drug product containers, and closures. These lots should be held back until appropriate testing or examination is conducted and they are deemed fit for use.

2.3 IN RESPONSE PROVIDE THE FOLLOWING: Analysis of the existing procedures employed by your organization, with a focus on their robustness and suitability. Implementation of provisions for QU oversight across all your operations. This oversight aims to assess the adherence to appropriate quality control practices throughout the organization. A comprehensive and conclusive review of every batch, along with its associated data and documentation, prior to making any QU disposition decisions.

- 2.4 CONCLUSION:** In summary, this letter outlines the need to assess and enhance the quality control processes within your organization, ensure continuous QU oversight, conduct rigorous batch reviews, and maintain strict oversight over investigations and other QU responsibilities to uphold the quality and integrity of your products.

CASE STUDY:3 ⁽⁷⁾

3.1 NAME OF COMPANY: LAAVO CLEAN , S.A. de C.V.

3.2 ISSUE: The FDA has found issues with two hand sanitizer products manufactured by LaavoClean.

Here are the key points:

1. LaavoClean KIDS Hand Sanitizer (Without Alcohol):

- Labeled as containing 0.13% of the active ingredient benzalkonium chloride (BZK).
- FDA testing found an average of 0.15% BZK, which is 115% of the label claim.
- This product is considered adulterated as it contains more BZK than stated on the label.

2. LaavoClean Hand Sanitizer (Without Alcohol):

- Labeled as containing 0.13% of the active ingredient BZK.
- FDA testing found two batches with an average of 0.15% and 0.12% BZK, which is 92.7% of the label claim for one batch.
- These products are considered adulterated as they do not meet the BZK content as declared on the label.

All of LaavoClean's hand sanitizers were detained and refused admission at the U.S. border and did not enter the United States. The FDA has not recommended removing these products from the market but has informed the public about the potency issues on their website.

3.3 IN RESPONSE PROVIDE THE FOLLOWING:

The FDA conducted a detailed investigation into the hand sanitizer products that were labeled as containing 0.13% BZK but actually contained different amounts:

1. LaavoClean KIDS Hand Sanitizer (Without Alcohol):

- Label claimed 0.13% BZK.
- FDA testing found an average of 0.15% BZK, exceeding the labeled amount.

2. LaavoClean Hand Sanitizer (Without Alcohol):

- Label claimed 0.13% BZK.
- FDA testing found two batches with an average of 0.15% and 0.12% BZK, falling below the labeled amount for one batch.

The FDA requested the following information from the manufacturer:

- A list of all raw materials used, including supplier names, addresses, and contact details.
- Details of any batches of hand sanitizer products shipped to the United States.
- A complete reconciliation of all distributed materials.
- Copies of batch records for any batches sent to the United States.

This information was likely requested to investigate the discrepancies in BZK content, ensure product quality, and trace the supply chain and distribution of these hand sanitizers.

3.4 CONCLUSION: The FDA conducted investigations into two hand sanitizer products manufactured by LaavoClean. These products were labeled as containing 0.13% benzalkonium chloride (BZK) but were found to have different BZK levels during FDA testing: one had more, and one had less BZK than claimed. The FDA requested information on raw materials, batches shipped to the U.S., reconciliation of distributed materials, and batch records from the manufacturer. This was done to assess the product quality, trace the supply chain, and ensure compliance with labeling claims.

CASE STUDY: 4 ⁽⁸⁾

4.1 NAME OF COMPANY: INTERNATIONAL CORP. LTD.

4.2 ISSUE: The company's firm failed to establish an adequate quality control unit with the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging materials, labeling, and drug products (21 CFR 211.22(a)).

The provided records show that your quality unit (QU) didn't effectively oversee the quality of your drug manufacturing operations, particularly in approving or rejecting materials in your system. This raises concerns that your QU may not be properly overseeing other important areas like production, facilities, lab controls, and packaging.

To address this, the FDA recommends following their guidance on implementing quality systems and risk management approaches outlined in the Quality Systems Approach to Pharmaceutical CGMP Regulations. This guidance can help you meet the requirements of CGMP regulations (21 CFR, parts 210 and 211). **4.3 IN RESPONSE PROVIDE THE FOLLOWING:** You need to create a thorough plan to make sure your quality unit (QU) can do its job properly. This plan should include:

1. Checking if your company's procedures are strong and suitable.
2. Making sure the QU keeps an eye on all your operations to ensure they follow the right practices.
3. Reviewing each batch and its info carefully before the QU makes a decision about it.
4. Having the QU oversee and approve investigations and other important tasks to guarantee the quality of your products.

4.4 CONCLUSION: This letter informs the company that there are violations at their facility, and it's their responsibility to investigate and fix them. FDA placed their facility on Import Alert 66-40 on August 7, 2023. They need to promptly correct these violations. FDA may delay approval of new applications or supplements listing their firm as a drug manufacturer until the violations are resolved and compliance is confirmed. FDA may also re-inspect to verify corrective actions. Failure to address violations may lead to FDA withholding Export Certificates and delaying approval for their firm as a drug manufacturer. The company has 30 working days to respond in writing, outlining the actions taken to address the violations and prevent their recurrence. If they need more time, explain the delay reasons and their completion schedule.

Case :5 [9]

1.1 Name of Company : Aurobindo Pharmaceutical Limited

1.2 Issue: Failure of your quality unit to ensure that critical deviations are investigated and resolved.

- The company does not fully investigate discrepancies. During method transfer for the gas chromatography–mass spectrometry (GC-MS), method for determination in , a starting material for , The company failed to pass the method transfer acceptance criteria for inter laboratory precision because of observed peak splitting.
- Although the company conducted an investigation, it was not adequate as company's investigation failed to consider all potential equipment sources. The failing result was invalidated without a scientific rationale and was not reported in the "problems faced" or "corrective actions taken" sections of the approved method transfer report.
- Ultimately, The Company attributed the failing result to a dirty and/or degraded column, replaced the column, and obtained a passing result with a fresh sample.
- Likewise, after attributing the failure to the deteriorated column, The Company did not establish controls to ensure that only acceptable columns would be used in future analyses.

1.3 Conclusion:

- Correct any deviations promptly. FDA may withhold approval of new applications or supplements listing your firm as a drug manufacturer until any deviations are completely addressed and we confirm your compliance with CGMP.
- We may re-inspect to verify that you have completed corrective actions to any deviations.

Case -6 [10]

2.1 Name Of Company: Centrient Pharmaceuticals India Private Limited

2.2 Issue: Failure to establish and follow written procedures for investigating critical deviations or the failure of API batches to meet specifications.

- The company failed to adequately investigate and determine the root cause of black particles in two batches of API.
- For example, the company investigation report for batch stated the black particles were non-metallic charred product residue. The company's report further indicated that the sample was observed by analysis to "dissolve in solution." However, during the inspection, they were unable to provide our investigator the data to support the conclusion. Well documented, thorough, scientifically sound investigations are necessary to identify the root cause in order to implement appropriate CAPAs.
- Their response indicates you installed to limit the presence of metal particles in the API. However, your investigation remains inadequate because they did not provide the data to support their proposed root cause or identify an adequate CAPA. For example, their CAPA does not address non-metallic sources of contamination, such as charred product residue or inadequate cleaning or fully address metallic sources of contamination, such as reactive, additive, or absorptive product contact surfaces.

2.3 In response to this letter:

- A comprehensive assessment and remediation plan to ensure your QMS is given the authority and resources to effectively function. The assessment should also include, but not be limited to
- A determination of whether procedures used by their firm are robust and appropriate.
- Provisions for QMS oversight throughout their operations to evaluate adherence to appropriate practices.
- A complete and final review of each batch and its related information before the QMS disposition decision.
- Oversight and approval of investigations and discharging of all other QMS duties to ensure identity, strength, quality, and purity of all products.

2.4 Conclusion:

- A complete assessment of documentation systems used throughout your manufacturing and laboratory operations to determine where documentation practices are insufficient. Include a detailed corrective action and preventive action (CAPA) plan that comprehensively remediates your firm's documentation practices to ensure you retain attributable, legible, complete, original, accurate, contemporaneous records throughout their operation.
- A comprehensive assessment and CAPA plan for computer system security and integrity. Include a report that identifies vulnerabilities in design and controls, and appropriate remediations for each of their laboratory computer systems.

Case :7[11]

3.1 Name of company: stason pharmaceuticals , inc.

3.2 Issue: violation of current good manufacturing practice cGMP for finished pharmaceuticals.

During the investigation observed specific violation and it is given below :

- The company failed to thoroughly investigate any unexplained difference or failure of batch or any of its components to meet any of its specification whether the batch is distributed or not. The company was not able to assure that your temozolamide capsules met dissolution attributes through its shelf life. We acknowledged that FDA approved their expanded dissolution specification but their response is inadequate because they did not determine the clear root cause of dissolution failure found in lot after the specification was revised.
- The company lacked adequate interim measures to address cleaning issues including a verification failure following the manufacturing of methotrexate tablets.

3.3 In a response to this letter:

- comprehensive assessment of overall system for investigating deviation complaints OOS results and failures and provide a detailed action plan for remedies. The company's action plan should include significant improvements in investigation competencies scope CAPA effectiveness and determination of root cause.

3.4 Conclusion:

- The company is responsible for investigating and determining the cause of violations and for preventing their recurrence and occurrence of other violation.

Case: 8 [11]

4.1 Name of company : R&B medical group inc.

4.2 Issue: significant deviation from the regulation for human cells, issues and cellular and tissue based product (HCT/PS)

FDA has found significant violation upon review of documents collected in inspection it include following:

- Failure to test using appropriate FDA- licensed approved or clear donor screening test in accordance with manufacturer's instruction to adequately and appropriately reduce risk of transmission of relevant communicable disease agents or diseases.
- Failure to establish and maintain a quality program that include investigation and documenting HCT/P deviation related to core HCT/P deviation.
- The deviation find above are not intended to be an all inclusive list of deficiency at their facility. it is the company's responsibility to ensure that responsibility to ensure that their establishment is compliance with all applicable statutory and regulatory requirements.
- The regulation at 21CFR 1271.8(d) specifically required the responsible person who is performing the donor eligibility determination to determine donor whose specimen test for communicable disease agent is reactive.

- In permeable to final rule published on 25th may 2004 the agency stated that confirmatory test are not as sensitive as screening test in detecting early infection.

4.3 Conclusion :

- The firm should maintain data of test performed and procedures by which they perform test should also be according to guideline and if any deviation occurs then it should be investigated.

Case: 9 [11]

5.1 Name Of Company : ACRX Specialty Pharmacy inc.

5.2 ISSUE: Drug product they produced failed to meet the condition of section 503A of the federal food, drug and cosmetic act (FDCA) [21 U.S.C.&353a] for exemption from certain provision of FDCA and serious deficiencies in their practice for producing sterile drug products which put patients at risk

- Section 503a of the FDCA describes the condition under which human drug products compounded by pharmacist in a state or federal facility or licensed physician.
- Failure to meet condition of section 503A for example the investigator noted your firm did not receive valid prescriptions for individually identified patients for a portion of drug products you produced.
- Therefore the products you produced does not meet the condition for section 503 A and are not eligible for exemptions in that section including FDA approved requirement under section 505 of FDCA.
- Investigator noted that drug products intended or expected to be sterile PA were prepared, packed, or held under insanitary conditions that may become contaminate and be injurious to health for example: the investigator observed poor practice during aseptic processing including door open between anteroom and unclassified area, your firm failed to establish environmental condition in aseptic area.
- Ineligible drug products are misbranded under section 502(f)(1) of FDCA
- Corrective action regarding it includes:

You state that you have committed to ceasing the practice of holding door between classified and unclassified areas and to perform regular pressure differential monitoring but you did not provide supporting document of correction.

Regarding your responses related to insanitary condition some of your corrective action appears deficient

5.3 Conclusion:

- The company is responsible for investigating and determining the cause of the violation and for preventing their reoccurrence or the occurrence of the other violation. It is their responsibility to ensure that their firms complies with all requirement of federal law including FDA regulation

Case:10 [11]

6.1 Name Of Company: Auro pharmacies, inc, Central Drug Compounding pharmacy

6.2 Issue: Drug products they produced fail to meet the condition of section 503A of the FDCA [21 US C. 353a] for exemption of the FDCA

- SECTION 503a of the FDCA describes the condition under which human drug products compounded by licensed pharmacy or federal facility or licensed physician.
- During the investigation FDA investigator noted that drug products produced by your firm fails to meet conditions of 503 A for example, your firm not receive the valid prescription for individually identified patient for non sterile dosage forms.
- Therefore the products you compounded does not meet the condition for section 503A and are not eligible for exemption in that section.
- FDA investigator observed vermin in your production area especially ants are observed on floor in pre gown room where non sterile hairnets and masks are donned prior classified to gowning room, Your ISO 5 classified PARU areas had visibly dirty equipments and surfaces.

→ Corrective actions for this includes:

- We acknowledged that your firm voluntarily ceases sterile production and also recalled all lots of drugs intended to be sterile that were within expiry due to lack of sterility assurance.
- Please be aware that section 501(a)(2)(A) of the FDCA concerning insanitary conditions applies regardless of whether the drug products meet the condition of section 503 A.

6.3 Conclusion:

- The company is responsible for investigating and determining the root cause of violation for preventing their reoccurrence and occurrence. It is their responsibility to ensure that their firm complies with all requirements of federal law including FDA regulations

Case:11 [11]

7.1 Name Of Company: Shen clinic, LLe

7.2 Issue: Unapproved and misbranded products related to corona virus disease (COVID-19).

- There is currently global outbreak of respiratory disease caused by novel coronavirus that has named as severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) This is caused by virus named corona virus disease 2019.
- On 3rd march 2020 president declared national emergency in a response to COVID outbreak so FDA is taking urgent steps protect consumers from certain products without that are without FDA approval calim to mitigate prevent and treatment of COVID-19.
- Some examples of claims that establish the intended use of your products and misleadingly represent them as safe and effective for treatment of COVID -19 Includes TCM vs COVID-19, it is old age method to treat fever and cough are used in corona as they were SARS epidemic of 2003.
- You should take immediate action to correct violation in this, it doesn't meant to be an all inclusive list of violation that exist in a connection with your products or operation.
- FDA advising consumers not to purchase or use certain products that have not been approved or authorized by FDA and that are being misleadingly represented as safe or effective for COVID-19.

7.3 Conclusion:

- The firm should take immediate action to correct violations once they have taken corrective action to cease the sale of your unapproved and unauthorized products for prevention mitigation and treatment.

CONCLUSION:

This article underscores the importance of managing deviations in pharmaceutical manufacturing. It highlights the consequences of non-compliance through case studies, emphasizing the need for robust quality control and corrective actions. In summary, a commitment to regulatory compliance and a culture of continuous improvement are vital in ensuring pharmaceutical product quality and safety.

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