檔　　號:
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衛生福利部食品藥物管理署 函

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受文者：中華民國製藥發展協會

發文日期：中華民國115年3月23日
發文字號：FDA品字第1151101814號
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密等及解密條件或保密期限：
附件：原料藥廠違反GMP警訊乙份 (A21020000I_1151101814_doc1_Attach1.pdf)

主旨：有關美國FDA發布美國原料藥廠Warning Letter乙案，請轉知所屬會員知照。

說明：

一、美國衛生主管機關Food and Drug Administration（FDA）查核印度原料藥廠「Flowchem Pharma Private Limited」（廠址：Plot No. 2B-2 & 2C, Survey No. 7(p) & 8 (p), Gollapuram Industrial Park, Hindupur Taluk, Andhra Pradesh, India），判定違反CGMP，並於115年3月11日發布Warning Letter（詳附件，115年3月17日公布於美國FDA官網）。

二、鑑於上述原料藥廠未符合GMP規定，具影響藥品製造品質之風險，請轉知所屬會員釐清國產及輸台製劑產品相關原料藥使用情形，並應依風險管理原則執行相關後續處置。

正本：中華民國西藥商業同業公會全國聯合會、中華民國西藥代理商業同業公會、台北市西藥代理商業同業公會、中華民國開發性製藥研究協會、台灣藥品行銷暨管理協會、台灣製藥工業同業公會、中華民國學名藥協會、中華民國製藥發展協會

副本：電子公文交換章 2026/03/23 13:16:12

WARNING LETTER

Flowchem Pharma Private Limited

MARCS-CMS 720719 — MARCH 11, 2026

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Delivery Method:
VIA UPS
Reference #:
320-26-51
Product:
Drugs

Recipient:
Mr. Anjan K. Roy
Managing Director
Flowchem Pharma Private Limited
No.: HIG-2000, Ray House
Yelahanka New Town
Bengaluru 560064 Karnataka
India

Issuing Office:
Center for Drug Evaluation and Research (CDER)
United States

Warning Letter 320-26-51

March 11, 2026

Dear Mr. Roy:

The United States Food and Drug Administration (FDA) inspected your drug manufacturing facility, Flowchem Pharma Private Limited, FEI 3019853324, at Plot No. 2B-2 & 2C, Survey No. 7(p) & 8(p), Gollapuram Industrial Park, Hindupur Taluk, Andhra Pradesh, from September 8 to 12, 2025.

This warning letter summarizes significant deviations from Current Good Manufacturing Practice (CGMP) for active pharmaceutical ingredients (APIs).

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your APIs are adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 351(a)(2)(B).

We reviewed your September 25, 2025 response to our Form FDA 483 in detail and acknowledge receipt of your subsequent correspondence.

Feedback

During our inspection, our investigators observed specific deviations including, but not limited to, the following.

1. Failure to clean equipment and utensils to prevent contamination or carry-over of a material that would alter the quality of the intermediates and API beyond the official or other established specifications.

Your firm manufactures **(b)(4)** API intended for the U.S. market. You lacked adequate procedures for cleaning and maintenance of manufacturing equipment. FDA documented an unidentified **(b)(4)** residue, apparent rust, and unidentified liquids inside or on product contact surfaces of various non-dedicated process equipment used in the production of **(b)(4)**. Each was marked as cleaned and ready for use. Additionally, investigators observed discolored and scratched **(b)(4)** containers for use in **(b)(4)** operations.

In your response, you state that you have cleaned equipment and have updated cleaning and maintenance procedures. You also commit to using **(b)(4)** storage for **(b)(4)**.

Your response is inadequate in that it fails to comprehensively address cleaning and maintenance deficiencies or how you will attempt to develop any system to proactively address these issues. Furthermore, you did not perform an assessment of residues and liquids in process equipment that you had identified as clean.

Inadequately cleaned and maintained manufacturing equipment can lead to potential cross-contamination that could compromise your API's quality and safety.

In your response to this letter, provide:

- Your corrective action and preventive action (CAPA) plan to implement routine, vigilant operations management oversight of facilities and equipment. This plan should ensure, among other things, prompt detection of equipment/facilities performance issues, effective execution of repairs, adherence to appropriate preventive maintenance schedules, timely technological upgrades to the equipment/facility infrastructure, and improved systems for ongoing management review.
- A comprehensive, independent retrospective assessment of your cleaning effectiveness to evaluate the scope of cross-contamination hazards. Include the identity of residues, other manufacturing equipment that may have been improperly cleaned, and an assessment whether cross-contaminated products may have been released for distribution. The assessment should identify any inadequacies of cleaning procedures and practices, and encompass each piece of manufacturing equipment used to manufacture more than one product.
- A CAPA plan, based on the retrospective assessment of your cleaning program, that includes appropriate remediations to your cleaning processes and practices, and timelines for completion. Provide a detailed summary of vulnerabilities in your process for lifecycle management of equipment cleaning. Describe improvements to your cleaning program, including enhancements to cleaning effectiveness; improved ongoing verification of proper cleaning execution for all products and equipment; and all other needed remediations.

2. Failure to ensure that materials are handled and stored in a manner to prevent degradation, contamination, and cross-contamination.

Your firm did not adequately prevent contamination of materials and intermediates. For example, you stored bags of raw materials outside your facility without adequate protection. Our investigators observed multiple bags of material, containing API, that were open and exposed to the environment. These bags were observed adjacent to an area undergoing apparent construction, an activity which may generate airborne dust and debris. Moreover, when your firm prepared a fresh solution of **(b)(4)**, our investigators observed that it was visibly contaminated with unidentified brown particulate matter on the surface.

Your response states that you have moved the storage location of **(b)(4)** and that you have developed a new procedure for preparing **(b)(4)** solutions in a **(b)(4)**, rather than in open barrels, as observed during the inspection. Your response is inadequate in that your response fails to identify or provide a comprehensive description of the current storage conditions of materials. Moreover, your response fails to comprehensively evaluate your material storage practices. You do not

address whether **(b)(4)** or any other materials and intermediates remain stored outside without adequate protection. Additionally, your response fails to identify the source of the contamination observed or provide any evidence that improperly stored materials were not adversely affected by their storage conditions.

The introduction of undesirable foreign matter into a raw material, intermediate, or API during production may adversely affect API quality. It is essential that API manufacturers take appropriate measures to prevent such contamination.

In your response to this letter, provide:

- Your CAPA plan to implement routine, vigilant operations management oversight of facilities and equipment. This plan should ensure, among other things, prompt detection of equipment/facilities performance issues, effective execution of repairs, adherence to appropriate preventive maintenance schedules, timely technological upgrades to the equipment/facility infrastructure, and improved systems for ongoing management review.
- Your plans to provide sufficient space for the orderly storage of materials and adequate protection from environmental elements.

3. Failure to establish an impurity profile for identified and unidentified impurities and failure to ensure all test procedures are scientifically sound and appropriate to ensure that your API conform to established standards of quality and purity.

You failed to conduct a comprehensive evaluation of your manufacturing processes to identify potential impurities. For example, you did not validate your method for testing for organic impurities in **(b)(4)** API, nor did you have a specification for these impurities. Chromatograms from your unvalidated method showed unknown, unintegrated impurities that were not quantified. As a result, these peaks were not fully considered when making your release decisions.

Additionally, you failed to determine the suitability of each secondary reference standard against a primary reference standard. For example, you continued to use your 2021 standard for **(b)(4)** that was never qualified against an official reference standard.

In your response, you state that you manufactured API as per the United States Pharmacopeia (USP) monograph and therefore did not test for impurities. Your response further states that you identified and synthesized potential impurities, and you commit to developing and validating an analytical method for organic impurities. This is unacceptable, as establishing an impurity profile for your API is expected under CGMP. Furthermore, your response is inadequate in that it fails to demonstrate whether released batches will meet your general specification for related substances, particularly given that your retrospective analysis includes up to **(b)(4)** unknown impurities.

Manufacturers are expected to establish complete impurity profiles for each API as part of the process validation effort. You are responsible for developing and using suitable methods to detect impurities when designing, and making changes to, your manufacturing processes. If you detect new or higher levels of impurities, you should fully evaluate the impurities and take action to ensure the drug is safe for patients.

In your response to this letter, provide:

- A comprehensive independent assessment of your laboratory practices, procedures, methods, equipment, documentation, and analyst competencies. Based on this review, provide a detailed plan to remediate and evaluate the effectiveness of your laboratory system.
- A retrospective review of all API lots released without appropriate testing for impurities and how that may impact finished drug quality.
- A plan to address any product quality or patient safety risks for out-of-specification lots of APIs in U.S. distribution, including recalls.
- Specifications, including test methods, used to release APIs. Your response should address your capability to detect and quantify a wide array of potential impurities or contaminants.
- Improved procedures for performing a systemic evaluation for identifying impurities and establishing a control strategy from the process development stages.

- Risk assessments for the potential presence of impurities in **(b)(4)** USP manufactured at your facility. Include your program for ongoing evaluation of impurity profiles for all drugs and starting materials you produce.
- Identify corrective actions to ensure adequate quality oversight of establishing appropriate impurity and degradant limits for all drugs and starting materials you produce, using well-studied, scientifically based impurity profiles specific to their own manufacturing processes.

4. Failure to test the identity of each batch of incoming production material and appropriately qualify suppliers to rely upon their Certificate of Analysis.

You failed to conduct an identity test on each lot of raw material used in the manufacture of your API. You instead relied on the certificates of analysis (COAs) from your supplier without adequately qualifying them.

For example, you accepted **(b)(4)** raw material without performing identity testing or performing vendor qualification. Your firm justified this lack of material testing by stating **(b)(4)**, which you stored outside your facility in open bags, was "**(b)(4)**." Moreover, you had not established an appropriate procedure for specification requirements of raw materials.

Your response discusses qualifying a new vendor for **(b)(4)** and develops a new procedure for setting raw material specifications. Your response is inadequate in that it fails to perform a retrospective analysis of materials that you accepted solely based on COAs. It also fails to address your practice of allowing some materials to be accepted based solely on COAs. Without adequate testing, there is no scientific evidence to assure that your raw materials conform to appropriate specifications before release.

In your response to this letter provide:

- A comprehensive, independent review of your material system, including but not limited to:
  o evaluating all suppliers of materials to determine if they are reliable and appropriately qualified;
  o an assessment of all materials to determine whether they are consistently of acceptable quality;
  o a review to ensure assigned expiration or retest dates are appropriate (supported by data)
  o adequacy of the supplier qualification program, and its selection, qualification, and disqualification provisions.
- Based on a thorough review, provide a summary of your systems CAPA to remediate the vendor qualification program and prevent use of unsuitable materials.
- The chemical quality control specifications, and associated justification for these specifications, you use to test and release each incoming lot of material for use in manufacturing.
- A description of how you will test each material lot for conformity with all appropriate specifications. If you intend to accept any results from your supplier's COA instead of testing each material lot, specify how you will robustly establish the reliability of your supplier's results through initial validation as well as periodic re-validation. In addition, include a commitment to always conduct at least one specific identity test for each material where such testing is required.
- A summary of results obtained from testing all materials to evaluate the reliability of the COA from each material manufacturer. Include your SOP that describes this COA validation program.

Quality Unit Authority

Significant findings in this letter indicate that your quality unit is not fully exercising its authority and/or responsibilities. Your firm must provide the quality unit with the appropriate authority and sufficient resources to carry out its responsibilities and consistently ensure drug quality.

CGMP Consultant Recommended

Based upon the nature of the deviations we identified at your firm, you should engage a consultant qualified to evaluate your operations and to assist your firm in meeting CGMP requirements. The qualified consultant should also perform a comprehensive six-system audit of your entire operation for CGMP compliance and evaluate the completion and efficacy of your corrective actions and preventive actions before you pursue resolution of your firm's compliance status with FDA.

See FDA's guidance document Quality Systems Approach to Pharmaceutical CGMP Regulations for help implementing quality systems and risk management approaches to meet the requirements of CGMP regulations 21 CFR, parts 210 and 211 at https://www.fda.gov/media/71023/download.

Your use of a consultant does not relieve your firm's obligation to comply with CGMP. Your firm's executive management remains responsible for resolving all deficiencies and systemic flaws to ensure ongoing CGMP compliance.

Conclusion

The deviations cited in this letter are not intended to be an all-inclusive list of deviations that exist at your facility. You are responsible for investigating and determining the causes of any deviations and for preventing their recurrence or the occurrence of other deviations.

FDA placed all drugs and drug products offered for import into the United States from your firm on Import Alert 66-40 on January 22, 2026.

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.

Failure to address any deviations may also result in the FDA continuing to refuse admission of articles manufactured at Flowchem Pharma Private Limited, Plot No. 2B-2 & 2C, Survey No. 7(p) & 8(p), Gollapuram Industrial Park, Hindupur, into the United States under section 801(a)(3) of the FD&C Act, 21 U.S.C. 381(a)(3). Articles under this authority that appear to be adulterated may be detained or refused admission, in that the methods and controls used in their manufacture do not appear to conform to CGMP within the meaning of section 501(a)(2)(B) of the FD&C Act, 21 U.S.C. 351(a)(2)(B).

This letter notifies you of our findings and provides you an opportunity to address the above deficiencies. After you receive this letter, respond to this office in writing within 15 working days. Specify what you have done to address any deviations and to prevent their recurrence. In response to this letter, you may provide additional information for our consideration as we continue to assess your activities and practices. If you cannot complete corrective actions within 15 working days, state your reasons for delay and your schedule for completion.

Send your electronic reply to CDER-OC-OMQ-Communications@fda.hhs.gov. Identify your response with FEI 3019853324 and ATTN: Andrew Haack.

Sincerely,
/S/

Francis Godwin
Director
Office of Manufacturing Quality
Office of Compliance
Center for Drug Evaluation and Research

CC:
Mr. Ravindra V. Kulkarni
Site Head
Flowchem Pharma Private Limited
Plot No. 2B-2 & 2C, Survey No. 7(p) & 8(p), Gollapuram Industrial Park
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