WARNING LETTER

Mentha & Allied Products Private Ltd.

MARCS-CMS 700242 — APRIL 16, 2025

More Warning Letters (/inspections-compliance-enforcement-and-criminal-investigations/compliance-actions-and-activities/warning-letters)

Delivery Method:
VIA EMAIL WITH READ RECEIPT
Reference #:
320-25-67
Product:
Drugs

Recipient:
Mr. Arvind Nanda
Joint Managing Director
Mentha & Allied Products Private Ltd.
16th Km Rampur-Swar Road
Rampur 244901 Uttar Pradesh
India

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

Warning Letter 320-25-67

April 16, 2025

Dear Mr. Nanda:

The United States Food and Drug Administration (FDA) inspected your drug manufacturing facility, Mentha & Allied Products Private Ltd., FEI 3004293613, located at 16th Km Rampur-Swar Road, Rampur, Uttar Pradesh, India, from September 16 to 25, 2024.

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 API is 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 December 10, 2024 response to our Form FDA 483 in detail. Your response is inadequate because you failed to provide supportive documentation for evaluation or adequate evidence of corrective actions taken to bring your operations into compliance with CGMP.

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

1. Failure to properly maintain buildings and facilities used in the manufacture of API.

Facility Conditions

You failed to maintain your drug manufacturing facility in a good state of repair. The washroom used by operators was observed to be heavily soiled, and soap for handwashing was not available. In addition, the gowning room was observed to have dirty lockers, garments, and operator shoes. Visibly soiled cloth gloves, which come into direct product contact with the **(b)(4)** USP **(b)(4)** API, were also observed in a supervisor's desk drawer to be used by operators during manufacturing. You reported that these gloves are cleaned after use; however, you lacked documentation to support their cleaning.

Equipment Cleaning and Maintenance

You failed to have adequate procedures for cleaning and maintenance of manufacturing equipment. For example, our investigators observed manufacturing equipment labeled as "cleaned" but found with the following deficiencies.

- A **(b)(4)** was labeled as clean and ready to be used; however, it was observed with residual product and a fraying rope inside the **(b)(4)**.
- A **(b)(4)** and **(b)(4)** were identified as cleaned; however, a significant amount of **(b)(4)** was observed on both pieces of equipment.
- Equipment and utensils (e.g., **(b)(4)** and **(b)(4)**), used to **(b)(4)** the **(b)(4)** USP **(b)(4)** API, were found to be stored on a dirty **(b)(4)** during the manufacturing of lot **(b)(4)**.
- **(b)(4)** were observed to be unclean, and these units lacked documentation of cleaning activities.

You also failed to adequately document and validate cleaning procedures. For example, your cleaning validation lacked details of the cleaning process (e.g., use of solvent or detergent, and description of critical cleaning steps). Sampling performed for microbial residues was identified to be from "different places" on the equipment and lacked specific sample locations and scientific rationale for their selection. In addition, you did not adequately document your equipment cleaning as part of the batch record or a cleaning record.

It is essential that your facility is in a good state of repair and sanitary conditions are maintained to avoid product contamination. Inadequately cleaned and maintained manufacturing equipment can lead to potential cross-contamination that could compromise your API's quality and safety.

In 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. Your plan should also ensure equipment is suitable for its intended use.
- 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 intermediates and API products.

2. Failure of your quality unit to exercise its responsibility to ensure the API manufactured at your facility are in compliance with CGMP.

Poor Documentation Practices

Your firm manufactures **(b)(4)** USP **(b)(4)** API. Your quality unit (QU) failed to implement adequate controls to ensure the integrity of data generated at your facility. Our investigators observed unacceptable documentation practices, including, but not limited to, the following: torn batch records, a torn testing chromatogram found in the manufacturing area uncontrolled labeling and clearance forms in the packaging area, and a partially completed labeling and clearance form in an unlocked desk drawer.

In addition, manufacturing batch records were initiated after the **(b)(4)** stage of the crude **(b)(4)** was completed. Your operators' practice was to backfill data that had previously been recorded on uncontrolled sheets for this initial API processing stage. These uncontrolled sheets were not maintained.

CGMP activities must be documented at the time of performance. Non-contemporaneous documentation on manufacturing records raises concerns about the validity and integrity of your firm's documentation practices and records.

Inadequate Electronic Data Controls

You failed to follow adequate controls for your computerized systems. For example, your computerized data backup procedure states that data is **(b)(4)** archived to a cloud server; however, data from the Agilent OpenLab Chromatographic Data System (CDS) was instead being archived **(b)(4)** to a second hard drive on the same computer. During the inspection, our investigators documented that the second hard drive was corrupted, and chromatographic data, obtained from February to September 2024, may have been affected.

You provided a document stating that the hard drive was sent to an external contractor for data recovery; however, you did not conduct a thorough investigation into this incident. Additionally, you failed to identify the specific data that may have been affected, including an evaluation of the potential impact on product quality.

Your quality system does not adequately ensure the accuracy and integrity of data to support the safety, effectiveness, and quality of the drugs you manufacture. See FDA's guidance document *Data Integrity and Compliance With Drug CGMP* for guidance on establishing and following CGMP compliant data integrity practices at https://www.fda.gov/media/119267/download.

In response to this letter, provide:

- A comprehensive assessment and remediation plan to ensure your QU is given the authority and resources to effectively function. The assessment should also include, but not be limited to:
  o A determination of whether procedures used by your firm are robust and appropriate.
  o Provisions for QU oversight throughout your operations to evaluate adherence to appropriate practices.
  o A complete and final review of each batch and its related information before the QU disposition decision.
  o Oversight and approval of investigations and discharging of all other QU duties to ensure identity, strength, quality, and purity of all products.
- A comprehensive investigation into the extent of the inaccuracies in data records and reporting including results of the data review for drugs distributed to the United States. Include a detailed description of the scope and root causes of your data integrity lapses.
- A current risk assessment of the potential effects of the observed failures on the quality of your drugs. Your assessment should include analyses of the risks to patients caused by the release of drugs affected by a lapse of data integrity and analyses of the risks posed by ongoing operations.
- A management strategy for your firm that includes the details of your global CAPA plan. The detailed corrective action plan should describe how you intend to ensure the reliability and completeness of all data generated by your firm including microbiological and analytical data, manufacturing records, and all data submitted to FDA.

3. Failure to test the identity of each batch of incoming production material and to 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 suppliers without adequately qualifying them. You tested **(b)(4)**, received as your primary raw material, for some quality attributes; however, an identity test was not performed before use in

manufacturing.

In addition, your procedure for vendor qualification states that critical vendors, such as suppliers of active raw materials, are required to be qualified. You did not qualify your suppliers of primary raw material and failed to establish the reliability of each of your suppliers' COA for raw material specifications and characteristics.

Without adequate testing, there is no scientific evidence to assure that your raw materials conform to appropriate specifications before release.

In response to this letter, provide a comprehensive review of your material system to determine whether all suppliers of raw materials are each qualified and the materials are assigned appropriate expiration or retest dates. The review should also determine whether incoming material controls are adequate to prevent use of unsuitable raw materials.

4. Failure to ensure that all specifications and test procedures are scientifically sound and appropriate to ensure that your API conform to established standards of quality.

*Inadequate Testing of **(b)(4)** API*

You failed to adequately test your **(b)(4)** USP **(b)(4)** API per the current USP monograph. For example, you did not conduct testing for "**(b)(4)**" and "**(b)(4)**." These tests are not required in your API specification. As a result, you distributed lots of **(b)(4)** API to the U.S. market without assurance that they meet the current USP standards. This may also render your **(b)(4)** USP adulterated under section 501(b) of the FD&C Act.

Inadequate Method Verification

You failed to perform an adequate analytical method verification for **(b)(4)** assay. Your protocol did not include an acceptance limit for the verification of the precision (percent relative standard deviation). The verification exercise included a single determination of each test.

Inadequate Stability Method Validation

You failed to ensure that the analytical method used for stability testing of **(b)(4)** USP **(b)(4)** API is suitable for its intended use. For example, you did not perform forced degradation studies to demonstrate that the method is stability-indicating.

In response to this letter, provide:

- A comprehensive assessment of your laboratory practices, procedures, methods, equipment, and documentation. Based on this review, provide a detailed plan to remediate and evaluate the effectiveness of your laboratory system.
- A list of chemical and microbial test methods and specifications used to analyze each lot of your drug product before making a lot disposition decision, and the associated written procedures.
- A comprehensive assessment and CAPA plan to ensure the adequacy of your stability program. Your remediated program should include, but not be limited to:
  o Stability indicating methods.
  o Stability studies for each drug product in its marketed container-closure system before distribution is permitted.
  o An ongoing program in which representative batches of each product are added each year to the program to determine if the shelf-life claim remains valid.
  o Detailed definition of the specific attributes to be tested at each station (timepoint).

5. Failure to demonstrate that your manufacturing process can reproducibly manufacture an API meeting its predetermined quality attributes.

Inadequate Process Validation

You failed to adequately validate your **(b)(4)** API manufacturing process. For example, your process validation lacked a scientific rationale for not including the smallest batch size your firm manufactures, a defined sampling plan for each stage, and testing requirements for raw materials used. In addition, your report lacked an evaluation of critical processing parameters results for the validation batches.

Equipment Qualification

You lacked qualification for major equipment, such as the **(b)(4)** tank, **(b)(4)** machine, and **(b)(4)**. In addition, the qualification of the **(b)(4)** lacked testing of the **(b)(4)** response to different types of metal, evaluation of its sensitivity to different sizes and types of **(b)(4)** particles, functionality of rejection mechanisms, and evaluation of operating conditions for different flow rates or product throughput. Furthermore, the qualification of the **(b)(4)** lacked a comprehensive range of operating parameters.

Without adequate process validation, your firm lacks basic assurance that you can reproducibly deliver products that meet specifications. See FDA's guidance for industry, *Process Validation: General Principles and Practices* for general principles and approaches that the FDA considers appropriate elements of process validation at https://www.fda.gov/media/71021/download. Adequate and complete equipment qualification is also critical to ensure process performance.

In response to this letter, provide your validation protocols and reports and critical equipment qualification protocols and reports. Also provide an update on the status of process performance qualification for your manufacturing processes for **(b)(4)** API for further distribution to the U.S. market and your program for ensuring an ongoing state of control of your manufacturing processes.

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 to assist your firm in meeting CGMP requirements.

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.

Cosmetics Manufactured for Distribution in the United States

In addition, some of the products you manufacture may be regulated as cosmetics, as defined in section 201(i) of the FD&C Act [21 U.S.C. 321(i)]. Any cosmetics you manufacture must comply with applicable statutory and regulatory requirements, including the FD&C Act. A cosmetic is deemed adulterated under section 601(c) of the FD&C Act [21 U.S.C. 361(c)] if it has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth or whereby it may have been rendered injurious to health. Some conditions that cause the drug products you manufacture to be adulterated may also cause any cosmetics you manufacture to be adulterated. We note that under section 301(a) of the FD&C Act [21 U.S.C. 331(a)], it is a prohibited act to introduce or deliver for introduction into interstate commerce a cosmetic that is adulterated. Further, your facility may be subject to requirements under the Modernization of Cosmetics Regulation Act of 2022 (MoCRA). You may find the FD&C Act, MoCRA, and FDA’s regulations through links on FDA’s website at https://www.fda.gov/cosmetics/cosmetics-guidance-regulation/cosmetics-guidance-documents.

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.

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 refusing admission of articles manufactured at Mentha and Allied Products Private Ltd., 16th Km Rampur-Swar Road, Uttar Pradesh, Rampur, India, 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 3004293613 and ATTN: Vilmary Negrón Rodríguez.

Sincerely,
/S/

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