WARNING LETTER

Tyche Industries Ltd

MARCS-CMS 693081 — FEBRUARY 06, 2025

Delivery Method:

Via Email

Reference #:

320-25-41

Product:

Drugs

Recipient:

Mr. Sandeep Gokaraju

Owner and Director

Tyche Industries Ltd

6-223, Sarpavaram (V)

Kakinada 533005 Andhra Pradesh

India

sandeepraju@tycheindustries.net (mailto:sandeepraju@tycheindustries.net)

Issuing Office:

Center for Drug Evaluation and Research (CDER)

United States

Warning Letter 320-25-41

February 6, 2025

Dear Mr. Gokaraju:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Tyche Industries Ltd, FEI 3004790309, at 6-223, Sarpavaram (V), Kakinada, from August 12 to 16, 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 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 4, 2024 response to our Form FDA 483 in detail and acknowledge receipt of your subsequent correspondence.

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

1. Failure to record all quality-related activities at the time they are performed.

Your quality unit (QU) failed to ensure the integrity of CGMP records. For example, during the inspection, a member of your management stated that two of your operators admitted to falsifying temperature data for a drying oven that was not turned on during the manufacture of a **(b)(4)** batch, which later failed to meet the residual solvents specification. In addition, an Assistant Manager in Production, an Assistant Manager in Quality Assurance, and a Quality Control Manager admitted to participating in the preparation of a “backdated calculation sheet” that was given to our investigator.

Your documentation practices were not indicative of a facility that is in compliance with CGMP.

Your response is inadequate. You state that you plan to hire a consultant to identify data integrity gaps and prepare and implement an action plan by June 30, 2025, approximately ten months from the conclusion of the inspection, which documented serious questionable data integrity practices. In addition, you state that you removed some of the employees involved in these incidents from CGMP-related activities, but you do not explain what was done to prevent the other employees involved in these activities from further data integrity deviations. Finally, you do not fully evaluate the scope of data integrity lapses at your firm, including by interviewing current and former employees and comprehensively reviewing data records.

Significant findings in this letter indicate that your QU is not fully exercising its authority and/or responsibilities. Your firm must provide the QU with the appropriate authority and sufficient resources to carry out its responsibilities and consistently ensure drug quality. For guidance on establishing and maintaining CGMP-compliant quality systems, see FDA’s guidances: *Q8(R2) Pharmaceutical Development* at https://www.fda.gov/media/71535/download, *Q9 Quality Risk Management* at https://www.fda.gov/media/167721/download and *Q10 Pharmaceutical Quality System* at https://www.fda.gov/media/71553/download. (https://www.fda.gov/media/71553/download.)

In your 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 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 your operation.

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

FDA documented rust-like residues inside **(b)(4)** non-dedicated **(b)(4)** used in the production of **(b)(4)**. In addition, FDA documented bare footprints inside another **(b)(4)** used in the production of **(b)(4)**. Each **(b)(4)** was labeled that it had been cleaned and was ready for use.

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

Your response is inadequate. You state that you reviewed the quality of the products manufactured in the impacted equipment since February 2024, but you do not describe how you conducted this review, nor the reason you limited your review to this timeframe. In addition, you do not adequately explain how you will prevent the failure to clean equipment after personnel enter inside it from recurring. Finally, you state that personnel entering inside equipment should “wear cloth shoe cover after removing shoe,” but failing to wear suitable clothing, including appropriate footwear, poses an unacceptable risk to the product.

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.
- 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.
- Your 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 for all products and equipment; and all other needed remediations.

3. Failure to test the identity of each batch of incoming production material.

Your incoming raw material used to manufacture API intended for the U.S. market was not adequately tested. For example, you did not test the **(b)(4)** used as a raw material in the production of **(b)(4)** for identity.

Your response is inadequate. You state that you "initiated the activity" to test **(b)(4)** for identity. However, you do not address whether all other raw materials are tested for identity or how you will prevent this deviation from recurring with new raw materials.

In your response to this letter, provide:

- A comprehensive, independent review of your material system to determine whether all suppliers of raw materials, containers, and closures, 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, containers, and closures.
- The chemical and microbiological quality control specifications you use to test and release each incoming batch of raw material for use in manufacturing.
- A description of how you will test each raw material batch for conformity with all appropriate specifications for identity, strength, quality, and purity. If you intend to accept any results from your supplier's certificates of analysis (COAs) instead of testing each raw material batch for strength, quality, and purity, 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 incoming raw material batch.
- A summary of results obtained from testing all raw materials to evaluate the reliability of the COA from each raw material manufacturer. Include your standard operating procedure that describes this COA validation program.
- A summary of your program for qualifying and overseeing contract facilities that test the drug products you manufacture.

Data Integrity Remediation

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. (https://www.fda.gov/media/119267/download.)

We strongly recommend that you retain a qualified consultant to assist in your remediation. In response to this letter, provide:

- 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.

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 products offered for import into the United States from your firm on Import Alert 66-40 on January 2, 2025.

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 Tyche Industries Ltd in Kakinada, 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 3004790309 and ATTN: Russell Riley.

Sincerely,
/S/

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

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