WARNING LETTER

Shimoga Chemicals

MARCS-CMS 727904 — JULY 13, 2026

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

Delivery Method:

VIA Electronic Mail

Reference #:

320-26-101

Product:

Drugs

Recipient:

Mr. C. Srinivas Rao

Partner

Shimoga Chemicals

W57A, MIDC, Kupwad

Sangli 416436 Maharashtra

India

Issuing Office:

Center for Drug Evaluation and Research (CDER)

United States

Warning Letter 320-26-101

July 13, 2026

Dear Mr. Rao:

The United States Food and Drug Administration (FDA) inspected your drug manufacturing facility, Shimoga Chemicals, FEI 3033881432, at W57A, MIDC, Kupwad, Sangli, Maharashtra, 416436, India, from January 19 to 23, 2026.

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 February 10, 2026, response to our Form FDA 483 in detail and acknowledge receipt of your subsequent correspondence.

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

1. Failure to ensure that all specifications, sampling plans, test procedures are scientifically sound and appropriate to ensure that your API conform to established standards of quality and purity.

Your firm manufactures the API, clomiphene citrate USP for U.S. distribution, intended for pharmacy compounding.

Data Integrity Concerns

Your firm failed to establish adequate controls over analytical testing data. Multiple instances of unreported sample injections for related substances and assay testing by high performance liquid chromatography (HPLC) were not documented in laboratory batch records. For example, clomiphene citrate USP batch CC/005/24-25 had an unreported injection with an out-of-specification (OOS) assay result of **(b)(4)**% (specification: **(b)(4)**%); however, the reported injection result of **(b)(4)**% was documented in the batch record. Additionally, because your firm lacked procedures for electronic data review and your quality unit (QU) did not review the electronic data, this batch was subsequently released and distributed to the U.S. market.

Without reliable analytical data, there is no assurance that distributed API batches meet identity, strength, quality, or purity specifications.

Your response is inadequate. In your response, you acknowledge undocumented trial injections, unreported analytical data, discarded printouts, and inadequate review of electronic laboratory records. You also commit to a retrospective review of all U.S. batches, including electronic data and documentation. You further mention hiring a third-party data integrity expert. However, your response does not describe a thorough retrospective investigation into the OOS result for batch CC/005/24-25 distributed to the U.S. market.

Sampling and Control Procedures Concerns

Your firm lacked adequate sampling procedures and records for clomiphene citrate USP in that batch records did not specify appropriate sampling instructions, quantities, or locations. For example, in **(b)(4)**-batches **(b)(4)**, the batch records do not specify the sample quantity, the location of sampling, the sampling method, or whether sampling occurred before or after **(b)(4)**. During the inspection, your production manager stated quality control (QC) samples were collected after **(b)(4)** the **(b)(4)**-batches, and samples were routinely collected from arbitrary locations from **(b)(4)**. Furthermore, your QC manager stated in-process testing occurred only when the owner provided samples.

Without defined and documented sampling instructions, testing results may be unreliable to confirm batch-to-batch quality or to detect manufacturing failures.

Your response is inadequate. You do not describe an adequate sampling program or an evaluation of the impact of inadequate sampling.

Method Verification Concerns

Your firm did not perform verification studies for any test methods, including but not limited to identification, related substances by HPLC, residual solvent, and assay by HPLC for clomiphene citrate USP. For example, your firm failed to verify the residual solvent method used by your contract testing laboratory. Additionally, during the inspection, your QC manager confirmed that no method verification has been performed for any of the test methods used for clomiphene citrate USP.

Unverified test methods may not accurately measure product quality attributes, and failing results may go undetected.

Your response is inadequate. In your response, you state you will validate your test methods and you will create a new procedure that ensures future methods will be validated. However, you do not discuss retrospective retain sample testing using appropriately verified methods by a qualified third-party laboratory.

In 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, independent review of all invalidated OOS (including in-process and release/stability testing) results for U.S. API for the last three years from the initial date of inspection, and a report summarizing the findings of the analysis, including the following for each OOS:
  o Determine whether the scientific justification and evidence relating to the invalidated OOS result conclusively or inconclusively demonstrates causative laboratory error.
  o For investigations that conclusively establish laboratory root cause, provide rationale and ensure that all other laboratory methods vulnerable to the same or similar root cause are identified for remediation.
  o For all OOS results with inconclusive or no root cause identified in the laboratory, include a thorough review of production (e.g., batch manufacturing records, adequacy of manufacturing steps, suitability of equipment/facilities, variability of raw materials, process capability, deviation history, complaint history, batch failure history). Provide a summary of potential manufacturing root causes for each investigation, and any manufacturing operation improvements.
- A comprehensive review and remediation plan for your OOS result investigation systems. The corrective action and preventive action (CAPA) should include but not be limited to addressing the following:
  o QU oversight of laboratory investigations
  o Identification of adverse laboratory control trends
  o Resolution of causes of laboratory variation
  o Initiation of thorough investigations of potential manufacturing causes, whenever a laboratory cause cannot be conclusively identified
  o Adequate scoping of each investigation and its CAPA
  o Revised OOS investigation procedures with these and other remediations
- A comprehensive, independent assessment of your in-process monitoring and sampling operations, focusing on each upstream process step that can introduce variability. Provide your remediation plan to improve: (1) in-process detection of variation, (2) upstream controls, and (3) sampling plans.
- Improved in-process testing and monitoring to enhance detection of variation during production of each batch. Include remediated in-process quality standards, including but not limited to enhanced sampling, that will more robustly monitor upstream process control. Describe how the improvements will ensure early detection of process variation and manufacturing defects, and prevent consumer exposure to substandard quality drug products.

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

Inadequate Process Validation

Your firm failed to establish adequate process validation for clomiphene citrate USP and its key starting materials. Your process validation reports do not accurately reflect actual manufacturing practices. For example, your validation reports fail to address the **(b)(4)** operation. Also, your validations do not address routine hold times. For example, **(b)(4)** batch **(b)(4)** was stored for approximately **(b)(4)** without defined hold-time limits or supporting studies.

Process validation evaluates the soundness of design and state of control of a process throughout its lifecycle. Each significant stage of a manufacturing process must be designed appropriately and assure the quality of raw material inputs, in-process materials, and finished drugs. Process qualification studies include intensive monitoring and testing throughout each significant process stage to characterize intra-batch variation and to evaluate batches to determine whether an initial state of control has been established. See FDA's guidance document *Process Validation: General Principles and Practices* for general principles and approaches that FDA considers appropriate elements of process validation at https://www.fda.gov/media/71021/download.

Successful process qualification studies are necessary before commercial distribution. Thereafter, ongoing vigilant oversight of process performance and product quality is necessary to ensure you maintain a stable manufacturing operation throughout the product lifecycle.

Your response is inadequate. You acknowledge the lack of appropriate process validation, and you commit to initiating validation protocols. You also state that a retrospective batch record review has been initiated for all clomiphene citrate USP batches shipped to the U.S. market. However, your response lacks sufficient details to determine whether your response is adequate. Specifically, you have not defined the scope of your record review, the acceptance criteria for your validation protocols, or the corrective actions to be taken if discrepancies are identified.

Inadequate Cleaning Procedures

Your firm also lacked robust and reproducible cleaning procedures for non-dedicated equipment used in the manufacture of the API clomiphene citrate USP, including **(b)(4)**. Specifically, your acceptance criteria for cleaning were not adequately defined and justified. Your cleaning procedures lacked specificity regarding cleaning methods, materials, contact times, and verification requirements. During the inspection, your firm's management stated that only "**(b)(4)** water" is used for all equipment cleaning regardless of product, which is inconsistent with your written cleaning procedures.

Without adequate cleaning validation, there may be a risk of cross-contamination between batches of API.

Your response is inadequate. In your response, you commit to performing a cleaning validation and risk assessment for shared equipment. However, you fail to provide adequate details regarding cleaning validation or an appropriate cross-contamination risk assessment for shared equipment.

In response to this letter, provide:

- A detailed summary of your validation program for ensuring a state of control throughout the product lifecycle, along with associated procedures. Describe your program for process performance qualification, and ongoing vigilant monitoring of both intra-batch and inter-batch variation to ensure a continuing state of control. Also, describe your equipment and facility qualification program.
- A timeline for performing appropriate process performance qualification for each of your marketed API. Also provide a risk assessment and any follow up actions to be taken for the distributed API produced without performing any process validation studies.
- Process performance protocol(s), and written procedures for qualification of equipment and facilities.
- Appropriate improvements to your cleaning validation program, with special emphasis on incorporating conditions identified as worst case in your drug manufacturing operation. This should include but not be limited to identification and evaluation of all worst-case:
  o Drugs with higher toxicities
  o Drugs with higher drug potencies
  o Drugs of lower solubility in their cleaning solvents
  o Drugs with characteristics that make them difficult to clean
  o Swabbing locations for areas that are most difficult to clean
  o Maximum hold times before cleaning

In addition, describe the steps that must be taken in your change management system before introduction of new manufacturing equipment or a new API.

- A summary of updated standard operating procedures that ensure an appropriate program is in place for verification and validation of cleaning procedures for API, processes, and equipment.

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

Investigation Handling

Your QU failed to ensure that discrepancies and potential OOS events were adequately investigated. Your firm has manufactured and distributed approximately **(b)(4)** batches since April 2023. While your firm has not documented any OOS investigations, out-of-trend investigations, or laboratory incidents over at least the last two years, during the

inspection, our investigators identified multiple events that should have triggered formal investigations, including the unreported OOS assay result for batch CC/005/24-25.

Without adequate investigations, quality failure may go undetected and unresolved.

Your response is inadequate. While you acknowledge discrepancies and potential OOS events were not adequately investigated, you do not provide a commitment to conduct any formal OOS investigation for batch CC/005/24-25.

Stability Program Deficiencies

Your QU failed to ensure that stability data adequately supports the assigned **(b)(4)** expiry date for clomiphene citrate USP. Your firm lacked raw test data, electronic or hardcopy, to support the results of your long-term stability study. In addition, while your stability management procedure requires that at least one commercial batch be placed on stability annually, your firm only placed batches on stability in 2021, 2022, and 2023. Your firm failed to place any U.S. batches manufactured in 2025 and 2026 on stability. Further, stability samples were stored in packaging that differed from the commercial container-closure system. This packaging has not been evaluated for equivalence.

Without complete stability data, there is no assurance that the API will maintain all quality attributes through expiry.

Your response is inadequate. You state that the ongoing stability study continues, but you fail to address the absence of raw data from the foundational 2015 study or your failure to place commercial batches on stability annually, as required by your own procedure.

CGMP Training Concerns

Your QU failed to ensure that manufacturing personnel were adequately trained. For example, an analyst who performed unreported injections lacked documented laboratory training and CGMP training. Additionally, no training records were available for a production operator who performed **(b)(4)** operations on a batch in U.S. distribution.

Using untrained personnel may create a systemic risk, potentially resulting in quality failures.

Your response is inadequate. You acknowledge the use of untrained or insufficiently trained personnel, but you provide only a general commitment to retraining. This commitment lacks a specific, documented training matrix, a training schedule, or qualification criteria for affected personnel.

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, independent 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
- Position descriptions that outline defined qualifications for key personnel, particularly within the QU, to confirm appropriate assignment of responsibilities.
- Evidence that trained skills are being applied in day-to-day operations, including any managerial oversight mechanisms used to verify on-the-job performance.

Your firm's quality systems are inadequate. For help implementing quality systems and risk management approaches to meet the requirements of CGMP regulations 21 CFR, parts 210 and 211, see FDA's guidance documents Quality Systems Approach to Pharmaceutical CGMP Regulations at https://www.fda.gov/media/71023/download, Q9(R1) Quality Risk

Management https://www.fda.gov/media/167721/download, and ICH Q10 Pharmaceutical Quality System at https://www.fda.gov/media/71553/download.

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*: Questions and Answers for guidance on establishing and following CGMP compliant data integrity practices at https://www.fda.gov/media/119267/download.

We acknowledge your commitment to engaging an independent third-party data integrity consultant to audit your operation and assist in meeting FDA requirements.

In response to this letter, provide:

- A comprehensive investigation into the extent of the inaccuracies in data records and reporting. Your investigation should include:
  o A detailed investigation protocol and methodology; a summary of all laboratories, manufacturing operations, and systems to be covered by the assessment; and a justification for any part of your operation that you propose to exclude.
  o Interviews of current and former employees to identify the nature, scope, and root cause of data inaccuracies. We recommend that these interviews be conducted by a qualified third-party.
  o An assessment of the extent of data integrity deficiencies at your facility. Identify omissions, alterations, deletions, record destruction, non-contemporaneous record completion, and other deficiencies. Describe all parts of your facility's operations in which you discovered data integrity deficiencies.
  o A comprehensive retrospective evaluation of the nature of the testing data integrity deficiencies. We recommend that a qualified third-party with specific expertise in the area where potential breaches were identified should evaluate all occurrences.
- 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. Your strategy should include:
  o A detailed corrective action plan that describes how you intend to ensure the reliability and completeness of all the data you generate, including analytical data, manufacturing records, and all data submitted to FDA.
  o A comprehensive description of the root causes of your data integrity lapses, including evidence that the scope and depth of the current action plan is commensurate with the findings of the investigation and risk assessment. Indicate whether individuals responsible for data integrity lapses remain able to influence CGMP-related or drug application data at your firm.
  o Interim measures describing the actions you have taken or will take to protect patients and to ensure the quality of your drugs, such as notifying your customers, recalling product, conducting additional testing, adding lots to your stability programs to assure stability, and enhanced complaint monitoring.
  o Long-term measures describing any remediation efforts and enhancements to procedures, processes, methods, controls, systems, management oversight, and human resources (e.g., training, staffing improvements) designed to ensure the integrity of your company's data.
  o A commitment to have a qualified consultant conduct extensive annual audits, for at least two years, to assist in evaluating CAPA effectiveness after you have executed your data integrity remediation protocol.
  o Inform FDA if you will be hiring a chief integrity officer who is fully empowered to receive anonymous complaints from employees reporting data integrity concerns and with the authority to ensure any potential breach is promptly investigated (by an independent quality assurance function, along with expertise from outside entities whenever needed).
- A status report for any of the above activities already underway or completed.

Drug Recall

On May 14, 2026, you issued a voluntary recall of clomiphene citrate USP due to deficiencies with your quality system and data integrity concerns. The company announcement was posted to the FDA website: https://www.accessdata.fda.gov/scripts/ires/index.cfm?Product=221115.

Additional API CGMP Guidance

FDA considers the expectations outlined in ICH Q7 when determining whether API are manufactured in conformance with CGMP. See FDA's guidance document Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients for guidance regarding CGMP for the manufacture of API at https://www.fda.gov/media/71518/download.

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 if your firm intends to resume manufacturing drugs for the U.S. market. 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 CAPA before you pursue resolution of your firm's compliance status with FDA.

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 June 2, 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 Shimoga Chemicals, at W57A, MIDC, Kupwad, Sangli, Maharashtra, 416436, 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 3033881432 and ATTN: Christopher M. Jenner.

Sincerely,
/S/

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

Was this page helpful? * (required)

Yes

No

Submit