



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE  
FOOD AND DRUG ADMINISTRATION

HFD-205  
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**WARNING LETTER**

CERTIFIED MAIL  
RETURN RECEIPT REQUESTED

WL No. 320-99-02

APR 8 1999

Mohan Chandavarkar  
Joint Managing Director  
FDC, Ltd.  
Roha, Maharashtra  
India

Dear Mr. Chandavarkar:

This is regarding an inspection of your active pharmaceutical ingredient (API) manufacturing facility in Roha, Maharashtra, India by the United States Food and Drug Administration from March 8-10, 1999. The inspection revealed significant deviations from U.S. good manufacturing practices in the manufacture of APIs, and resulted in the issuance of an FDA Form 483 to you at the completion of the inspection. These deviations cause these APIs to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act. Section 501(a)(2)(B) of the Act requires that all drugs be manufactured, processed, packed, and held according to current good manufacturing practice. No distinction is made between active pharmaceutical ingredients and finished pharmaceuticals, and failure of either to comply with CGMP constitutes a failure to comply with the requirements of the Act.

Specific areas of concern include, but are not limited to:

1. Laboratory procedures were not sufficient to assure that APIs conform to appropriate standards of identity, quality, purity, and stability. For example:

Testing for Organic Volatile Impurities was reportedly conducted by the USP method, but did not follow USP 23 in that replicate injections were not performed and relative standard deviation was not calculated.

[ ] testing for [ ] is not performed at the temperature indicated by USP 23. The temperature is not controlled nor measured during the test.

System suitability was not performed and there were no chromatograms of standard injections for the API or impurities for the forced degradation studies conducted as part of the validation of stability indicating methods.

Standard Operating Procedure No [ ] on Investigation of Out of Specification Data allows the acceptance of material with OOS results after duplicate analysis of a resample only, even when no sampling or testing errors are found.

2. Laboratory records were incomplete, for example:

Testing records did not always document testing operations such as sample, standard, or resolution solution, and calculations. Documentation of [ ] studies did not include the dates the sample was under stress conditions, or the criteria for evaluating the results as stability indicating. Analysts also recorded raw data on uncontrolled loose analytical sheets.

Reference standards were not adequately labeled and no receiving and testing records were available.

The lack of complete raw data for each analysis and the lack of complete records on reference standards raises questions about the reliability of all tests conducted and results obtained.

3. Batch production records were incomplete or inaccurate in that they did not include complete drying times, holding and transfer procedures, and heating/cooling times and temperatures, and in one case listed a different reactor vessel than that actually used.
4. Recovered solvents were not adequately controlled in that a drum of recovered [ ] was observed stored in the area identified for storage of recovered [ ]
5. Individual batches and recovered [ ] batches were not stored under controlled temperature and humidity conditions, and one container was observed torn with the contents spilling out.
6. The production of [ ] used in early stages of API manufacture, reprocessing, and equipment cleaning was not adequate to assure that the [ ] is suitable for its intended uses in that:

The system was not adequately designed and maintained to minimize [ ] areas and several sections were observed to be leaking. The system relies on [ ]

Routine monitoring of [ ] for [ ] testing was only performed on one sample composited from three points of use in different buildings. The samples were not collected as required in the sampling SOP, and the microbiological testing did not employ the most appropriate growth media. [ ] testing was not performed on [ ]

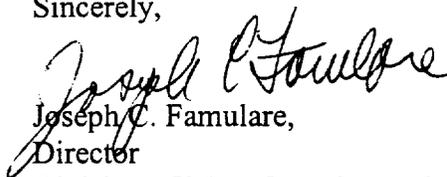
We have not received a response to the FDA-483 issued during the inspection. The above deficiencies are not to be considered as an all-inclusive list of the deficiencies at your facility. FDA inspections are audits which are not intended to determine all deviations that exist at a firm. If you wish to continue manufacturing APIs for use in the U.S., it is the responsibility of your firm to assure compliance with U.S. standards of good manufacturing practice for active pharmaceutical ingredients. We note that similar deficiencies regarding Laboratory Controls and Batch Production Records were observed during previous inspections in 1994 and 1997. We recommend that you evaluate your facility on an overall basis for CGMP compliance.

Until the FDA reinspects your facility and confirms that these deficiencies have been corrected, this office will recommend disapproval of any applications listing your firm as a manufacturer of APIs. If corrections are not initiated promptly, any API manufactured by your firm may be denied entry into the United States.

Please direct your written response to the issues discussed in this letter to Compliance Officer John M. Dietrick at the address shown above. Please reference CFN# 9611129 within your written response.

To schedule a reinspection of your facility after corrections have been completed, send your request to: Director, International Drug Section, HFC-133, Division of Emergency and Investigational Operations, 5600 Fishers Lane, Rockville, Maryland, 20857. You can also contact that office at (301) 827-5655 or by FAX at (301) 443-6919.

Sincerely,



Joseph C. Famulare,  
Director

Division of Manufacturing and Product Quality  
Center for Drug Evaluation and Research