



DEPARTMENT OF HEALTH & HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
FOOD AND DRUG ADMINISTRATION

PHILADELPHIA DISTRICT

D 10453

11/5/98

WARNING LETTER

98-PHI-09

January 6, 1998

900 U.S. Customhouse  
2nd and Chestnut Streets  
Philadelphia, PA 19106  
Telephone: 215-597-4390

CERTIFIED MAIL  
RETURN RECEIPT REQUESTED

Henry Jakubowski, President and General Manager  
Particle Size Technology, Inc.  
1930 Kumry Road  
Quakertown, PA 18941

GEN.	SPEC.
RELEASE	
F# _____	DATE <u>1/12/98</u>
Reviewed by <u>Kay M. English</u>	

Dear Mr. Jakubowski:

From November 12-20, 1997, Philadelphia District Investigator Debra J. Bennett conducted an inspection of your contract micronizing operation. At the conclusion of the inspection, she presented form FDA 483, Inspectional Observations, to you and discussed those observations with you. These observations represent serious deviations from current good manufacturing practices (CGMP's) with respect to the active pharmaceutical ingredients (API's) you process. Section 501 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) mandates that processing of drugs be performed in conformance with CGMP's to assure their safety, quality, and purity. The following observations cause API's micronized by your firm to be adulterated within the meaning of Section 501(a)(2)(B) of the FD&C Act:

1. Failure to have a validated cleaning procedure for multi-purpose micronizing equipment in the pharmaceutical processing area to ensure the absence of residual process materials and cleaning agents.

During the summation meeting held at the conclusion of the inspection, your management maintained that sampling and testing conducted by one of your clients should be adequate to show that your firm's equipment cleaning procedures are satisfactory for all of the API's processed by your firm. Such testing does not relieve your firm of the responsibility for demonstrating the validity of equipment cleaning procedures.

The FDA expects micronizers of API's to verify that cleaning procedures for multiple use equipment will remove residues of previous products and cleaning solvents/detergents to acceptable levels. Cleaning validation studies should be conducted following a written validation protocol that addresses who is responsible for performing and approving the validation study, includes acceptance criteria, and specifies when revalidation will be required. The validation protocol should also list: (1) the specific solvents or cleaning materials to be used; (2) the sampling plan and periodic testing to be conducted to assure that equipment surfaces have been appropriately cleaned; (3) the



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description and sensitivity of the analytical methods used; and (4) appropriate residue limits for each piece of equipment. Please refer to the enclosed *FDA Guide to Inspections of Validation of Cleaning Processes* for additional guidance.

2. Failure to validate the compressed air system that provides process air for propelling products through the mill and the cyclone filter.

The inspection revealed that the compressed air system serving the [REDACTED] mills in the "GMP" micronizing rooms has not been validated to prove that the system can produce oil-free and moisture-free filtered compressed air to reduce the risk of API contamination during the milling process.

In addition, the inspection disclosed that compressed air is produced by lubricated compressors in lieu of oil-free (non-lubricated compressors) and that your firm utilizes a lubricant not approved for use in food contact equipment. Lubricated compressors inherently discharge some liquid oil (in aerosol form) and oil vapor into the compressed air lines as a result of mechanical shearing, vaporization, and condensation of the lubricating oil film caused by the compression process. This oil often combines with moisture and rust in non-stainless steel compressed air distribution lines to produce a microbial growth supporting liquid that, if not adequately removed, can contaminate API's during the micronizing process.

During the summation meeting, your management claimed that compressed air is passed through a [REDACTED] filter before coming in contact with API's and that this equipment is used to remove any moisture in the air. The performance specifications for the [REDACTED] states that this equipment is designed to remove both oil and water aerosols from a compressed air system. Please submit validation data showing that your compressed air generation and distribution system is capable of producing oil and moisture-free filtered air when using lubricated compressors.

3. Failure to calibrate, and to have procedures that ensure the calibration of, analytical equipment.

The inspection revealed that the particle size analyzers used for both in-process and release samples are not calibrated and that there are no procedures in place to provide for and document periodic calibration. Additionally, the inspection found that there is no documentation to support that these analyzers have been qualified to ensure that they are appropriate for their intended uses and provide results that are accurate and reproducible.

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4. Failure to have an adequate air handling system to minimize the potential for cross-contamination.

During the inspection, Investigator Bennett observed dust on the loading pallets and floor outside the upper portion of "GMP" processing room -- as well as on the floor outside of "GMP" processing room -- in which sodium phosphate was being processed. This observation takes on special significance should you utilize more than one "GMP" processing room at a time as the dust may migrate into the other "GMP" rooms and become a potential contaminant.

Investigator Bennett also noted that heated and cooled air is supplied to your plant via a ceiling pipe that delivers air to the industrial side of the plant. She observed that a garage door in the concrete wall that separates the industrial micronizers from the "GMP" micronizers is kept open to allow the heated or cooled air to circulate throughout the plant and that the industrial micronizers are not completely enclosed. This layout, coupled with the fineness of micronized materials and their propensity to coat everything and everyone with which they come into contact, provides a potential for cross-contamination which could be increased should the exhaust fans in the "GMP" processing rooms be running when the processing room doors are open. You should ensure that your plant has an air handling system that contains dust from processing operations and minimizes the potential for cross-contamination from both API's and industrial chemicals.

The above is not intended to be an all-inclusive list of deficiencies at your firm. As top management, it is your responsibility to assure that all of your company's operations are in compliance with the FD&C Act and its associated regulations.

Federal agencies are advised of the issuance of all Warning Letters about drugs and devices so that they may take this information into account when considering the award of contracts.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. These actions include, but are not limited to, seizure and/or injunction.

Please advise this office in writing within fifteen (15) days of receipt of this letter as to the specific actions you have taken or intend to take to correct these violations. Your reply should

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be directed to the attention of Karyn M. Campbell, Compliance Officer, at the address noted on the letterhead.

Sincerely,



Diana J. Kolaitis  
District Director

Enclosure

cc: Robert E. Bastian, Director  
Division of Primary Care and Home Health Services  
PA Department of Health  
132 Kline Plaza, Suite A  
Harrisburg, PA 17104