



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service  
Mid-Atlantic Region

D1082B

Telephone (201) 331-2909

Food and Drug Administration  
Waterview Corporate Center  
10 Waterview Blvd., 3rd Floor  
Parsippany, NJ 07054

January 10, 1997

**WARNING LETTER**

Kenneth I. Sawyer  
President & CEO  
Par Pharmaceutical, Inc.  
One Ram Ridge Road  
Spring Valley, New York 10977

**File No: 97-NWJ-15**

Dear Mr. Sawyer:

During an inspection of your manufacturing facility located at 12 Industrial Avenue, Upper Saddle River, New Jersey on November 12 - December 10, 1996, investigators from this office, documented deviations from Current Good Manufacturing Practice Regulations (cGMPs), Title 21, Code of Federal Regulations (CFR), Parts 210 & 211. These deviations, regarding the production of Megestrol Acetate Tablets, 20mg & 40mg, were noted on the FDA483, List of Inspectional Observations, issued to your firm at the close of the inspection.

The above stated inspection revealed that your product, is considered to be adulterated within the meaning of Section 501 (a)(2)(B) of the Federal Food, Drug and Cosmetic Act (the Act), in that the methods used in, or the facilities and/or controls used in manufacturing are not in conformance with cGMPs:

- 1) Your firm failed to conduct a complete investigation and effective corrective measures to prevent the occurrence of microbiological contamination (including yeast and mold) in finished products, for example:

Between October 1995 to September 1996, ten batches failed established microbiological specifications. Your firm did not take immediate action to determine the cause of these failures. There is no assurance that every batch made between this period met internal microbial specifications, since testing was conducted on every 5th batch produced between February 8 to March 25, March 30 to May 9 and May 28 to June 15, 1996. This periodic monitoring continued even after there was evidence of *Klebsiella pneumoniae* in 3 lots produced within these time periods.

Additionally, your investigation attributed the presence of *Klebsiella pneumoniae* in two batches, to contamination in the [REDACTED]. However, an additional lot indicated the presence of *Klebsiella*, even after the installation of a new [REDACTED].

**RELEASE**

REVIEWED BY Mercedes Plotz 1/12/97

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- 2) Your firm failed to assess all potential environmental factors that could have an impact on the microbiological conditions in your facility.

The environmental monitoring study conducted by your firm to determine the source of yeast/mold contamination found in six batches, did not provide conclusive information on the source of the contaminant. Significant counts were found in the loading dock, drying oven room, cafeteria and raw material weighing room. There was insufficient testing of employee clothing or work areas to support the conclusion that the spread of contamination was attributed to employee movement.

There was no immediate response to the disruption in air flow, found during routine preventive maintenance of the air handling system in September 1996, even though this could have been a potential cause of microbiological contamination. Additionally, the air handling system has not been qualified, nor have modifications to this system, made in 1991, been evaluated.

- 3) The flow of raw materials used in-process and bulk tablets is inadequate to control microbial contamination.

For example, there is direct access from the loading dock to the oven drying room, which is a likely source of yeast and mold contamination in unprotected products.

Additionally, there is no documentation to support adequate sweeping and sanitation of floors in the warehouse, oven drying room, production areas and loading dock. Caddies used to transport materials throughout the plant, were not properly cleaned.

- 4) There was no assurance that raw material used in production met microbial specifications, for example there was no investigation regarding the failure of [REDACTED], during retest (Lot 20717, initially passed).

It was noted that your firm does not employ alert limits as an added control to assure that raw materials with high bacteria levels are not used in production.

We are in receipt of your written response, dated January 3, 1997, to the FDA483 issued on December 10, 1996. We agree with your position that it is unrealistic to exclude microorganisms ubiquitous to both physical environment and human beings in non-sterile dosage forms and facilities. However our concern with the

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evidence of microbiologic contamination in this particular product, lies with its indication for use in patients that are already immunologically depressed.

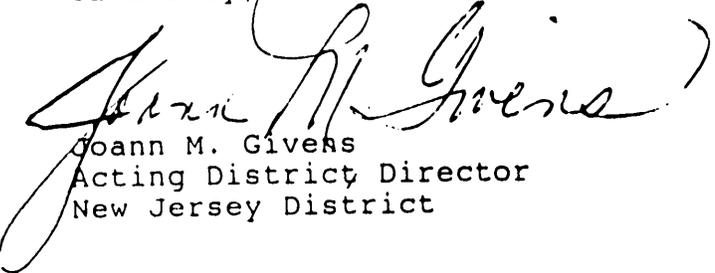
We consider your plans to construct physical restrictions to prevent the potential back flow of air from the loading dock to the oven drying room, to be a positive step in controlling a potential source of contamination. We also acknowledge your commitment to continue microbiological testing of every batch to demonstrate if your planned corrections are effective.

The procedures submitted with your response appear adequate, however a reinspection will be necessary to verify your planned corrective measures. There are several procedures mentioned in your response to FDA483 items 2, 6c and 7b, that were not included, and therefore could not be reviewed.

The above list is not intended to be all-inclusive of deficiencies at your facility. It is your responsibility to ensure that the drug products you manufacture are in compliance with the Act and regulations promulgated under it. Federal agencies are routinely advised of Warning Letters issued so that they may take this information into account when considering the award of contracts. You should take prompt action to correct these deficiencies. Failure to implement corrective measures may result in regulatory action, including seizure and/or injunction, without further notice.

You should notify this office in writing, within 15 working days of receipt of this letter, of the specific steps you have taken to correct the noted deficiencies, including an explanation of each step being taken to prevent the recurrence of similar conditions. If corrective action cannot be completed within 15 working days, state the reason for the delay and the timeframe within which corrections will be completed. Your reply should be sent to the New Jersey District Office, FDA, 10 Waterview Blvd., 3rd Floor, Parsippany, New Jersey 07054, Attention: Mercedes B. Mota, Compliance Officer.

Sincerely,

  
Joann M. Givens  
Acting District Director  
New Jersey District

**CERTIFIED MAIL -**  
**RETURN RECEIPT REQUESTED**