



CBER-99-19

Food and Drug Administration
Center for Biologics Evaluation
and Research
1401 Rockville Pike
Rockville MD 20852-1448

WARNING LETTER

APR 29 1999

CERTIFIED -- RETURN RECEIPT REQUESTED

Bosco T. Fong
President and COO
Peninsula Laboratories, Inc.
601 Taylor Way
San Carlos, CA 94070

Dear Mr. Fong:

The Food and Drug Administration (FDA) conducted an inspection of Peninsula Laboratories, Inc., 611 Taylor Way, Belmont, CA, between November 16-20, 1998. During the inspection, the FDA investigator observed significant violations of Section 351(a) of the Public Health Service Act (PHS Act) and the applicable standards and requirements of Subchapter F, Part 600, Title 21, Code of Federal Regulations (21 CFR), and your product license, as follows:

1. Operations were not in conformance with the commitments in your approved license, in that:
 - a. Packing, pre-treatment, cleaning, reconditioning, and storage of the _____ which is used during the manufacture of Human Immunodeficiency Virus Type 1 (For Further Manufacturing Use) _____ has not been validated.
 - b. Identification of microorganisms that are detected during bioburden testing is not performed. For example, surface bioburden testing performed on the purification/lyophilization room disclosed results as TNTC (too numerous to count). No further investigation was conducted.
2. Failure to determine if test results for finished product testing performed on or about October 1998, of lots 036957 and 06960 met the test objectives, in that an expired reference standard of _____ lot 036441, was used during _____ purity testing [21 CFR 610.1].

3. Failure to inform FDA about changes in the production process prior to implementation [21 CFR 601.12], in that a license supplement for the Rework Policy, SOP _____ was not submitted to FDA for review and written approval. The Rework SOP provides for reworking rejected product so that it will meet product specifications.
4. Failure to document, concurrently with the performance, each step in the manufacture and distribution of products [21 CFR 600.12(a)], in that:
 - a. Microbial level results and cleaning/sanitizing schedules are not maintained for the carboy, which is being used to store and transport USP Purified Water for final rinse of cleaned glassware;
 - b. There is no documentation that the following maintenance and procedures were performed at the frequencies prescribed in standard operating procedure (SOP) _____ entitled "Maintenance and Service Requirements for the _____"
 - i. _____ replacement of the deionized tank;
 - ii. _____ service of the reverse osmosis unit and carbon tanks;
 - iii. _____ replacement or service of the _____ cartridges;
 - iv. _____ service of the _____ units;
 - v. _____ monitoring of the Reverse Osmosis tank and discharge pressures; and
 - vi. _____ monitoring of conductivity at the sampling/point of use ports.
 - c. There is no validation report for the glassware rinsing study performed in May 1998;
 - d. There is no documentation demonstrating that the amount of residual peptide is not more than _____
 - e. There is no documentation that the analytical method for _____ was validated;
 - f. There is no documentation that Total Organic Carbon and conductivity testing was performed on the USP Purified Water.
5. Failure to ensure that precautions are taken to exclude extraneous infectious agents from manufacturing areas [21 CFR 600.11(a)], in that the current procedure entitled "Work Area Disinfection and Routine Cleaning," is not followed. For example, _____ are used during cleaning of the work areas and laboratory benches. The procedure states that cleaning agents approved for use in cleaning work areas are _____

6. Failure to ensure that all surfaces that come in contact with products are clean and free of surface solids, leachable contaminants, and other materials that will hasten the deterioration of the product or otherwise render it less suitable for the intended use [21 CFR 600.11(b)], in that the current procedure entitled "GMP Glassware Segregation, Cleaning, and Release Procedures for Building 611," is not followed. For example, _____ is currently used as a cleaning material in the procedure for hand washing of glassware. However, the procedure states that the only materials which are approved for use in cleaning glassware include _____
- _____ Additionally, there is no documentation to demonstrate that _____ is effective in removing product from glassware.

The above violations are not intended to be an all-inclusive list of deficiencies at your establishment. It is your responsibility, as management, to ensure that your establishment is in compliance with all requirements of the federal regulations.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. Such action includes license suspension and/or revocation, seizure and/or injunction, and/or civil penalties. 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.

We acknowledge receipt of your January 4, 1999, response to the Form FDA-483, that was issued at the conclusion of the most recent inspection of your firm. We have completed our review of your response and have determined that your responses are inadequate to address all the violations that FDA documented at your firm. Our evaluation of your responses follows and is numbered or labeled to correspond to the items as they appeared on the Form FDA-483 and in your responses:

- 3, 6, 12, 13, 16, 19 & 20 You have proposed to perform corrective actions to address the noted observations however, we question the completion dates which you have projected for completing these corrections. Please provide the rationale for these completion dates.

You should notify this Office in writing, within 15 working days of receipt of this letter, of additional or specific steps you have taken to correct the noted violations and to prevent their recurrence. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Your reply should be sent to the Food and Drug Administration, Center for Biologics Evaluation and Research, HFM-600, Suite 200N, 1401 Rockville Pike, Rockville, Maryland 20852-1448, Attention: Division of Case Management, HFM-610.

Sincerely yours,

A handwritten signature in cursive script that reads "Deborah D. Ralston".

Deborah D. Ralston
Acting Director
Office of Regional Operations