



DEPARTMENT OF HEALTH AND HUMAN SERVICE

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Public Health Service
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Food and Drug Administration
Baltimore District Office
900 Madison Avenue
Baltimore, MD 21201-2199
Telephone: (410) 962-3461 x122
FAX: (410) 962-2219

February 12, 1999

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Lawrence Loomis, President
New Horizons Diagnostics Corporation
9110B Red Branch Road
Columbia, Maryland 21045

Dear Mr. Loomis:

A Food and Drug Administration (FDA) inspection, conducted January 5-15, 1999 at your Columbia, Maryland manufacturing facility, determined that you manufacture *in vitro* diagnostic devices (IVD). IVDs are devices as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

During our inspection, deviations from the Quality System Regulation (QSR) requirements (Title 21, Code of Federal Regulations (CFR), Part 820) were observed. These deviations cause your devices to be adulterated within the meaning of Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for, manufacturing, processing, packing, storage, or holding, are not in conformance with current good manufacturing practice (CGMP) regulations. Please note that the QSR replaced the CGMP regulations for devices.

The deviations included the following:

- Failure to validate or to document adequately the validation of all processes, including, but not limited to, filtration, filling, cleaning, the effectiveness of antimicrobial agents, and the establishment of a microbial assurance level.
- Failure to develop, conduct, control, and monitor production processes to ensure that the devices conform to specifications, including, but not limited to, cleaning, limiting the number of culture passages, and environmental monitoring.
- Failure to establish acceptance procedures to ensure that specified requirements for pooled lots of antibody meet established specifications including, but not limited to, establishing stability and expiration date.

- Failure to ensure that device packaging is designed and constructed to protect the device from alteration or damage during the customary conditions of processing, storage, handling, and distribution.
- Failure to establish and maintain procedures to calibrate all measuring equipment routinely.
- Failure of quality audits and management reviews to ensure that the quality system is in compliance with the QSR regulations and your quality policy and objectives.

At the conclusion of the inspection, Mr. David P. Trudil, Executive Vice President, was given a written list of inspectional observations (FDA-483) which was discussed with him.

We acknowledge that you responded to the FDA-483 in a letter dated January 25, 1999. Observation 10 was corrected and verified at the discussion at the end of the inspection. Your responses to observations 2 and 9 appear adequate, but do not include a schedule for their completion. We consider the responses to the remaining observations to be inadequate for the following reasons:

- Regarding your responses to FDA-483 items 1, 3, and 4, validation entails establishing documented evidence that provides a high degree of assurance that a process will consistently produce a product that meets its specifications. Historic data alone cannot replace a properly designed validation study. Additionally, failure to validate has been a recurring inspectional observation beginning in March 1991. Therefore, please specify all procedures and processes you will validate and the expected completion dates for these studies. Additionally, the validation plan should address periodic re-validation.
- Regarding the antimicrobial preservatives effectiveness testing (FDA 483 item 3), it appears that it was performed in trypticase soy broth and not in the actual components that comprise your products. While this gives a general indication of the effectiveness of these preservatives, it does not assure effectiveness in the specific components in your IVDs. We cannot determine the protocol, source of samples, raw data, or interpretation of the results from the [REDACTED] document (Attachment 2 of your response) and, therefore, cannot determine whether this pertains to antimicrobial preservative effectiveness testing.
- Regarding packaging (FDA-483 item 5), your response stated that you would only review packaging concerns for new products. Please advise us of your intentions for examining packaging suitability of existing products.
- You assert in your response to item 6 that your product is a microbiologically uncontrolled device. This is contradicted by the specification of a microbial limit of [REDACTED] colony forming units, by the use of filtration through [REDACTED] micron filters, and by including antimicrobial agents in your products. These measures are used to control microbial contamination in an IVD and make your device a microbiologically controlled device. Please inform this office of your plans to validate these procedures and processes and the estimated date of completion.

- The issue of pooling expired reagents (FDA-483 items 7 and 8), for example, the antibody reagent, has also been an ongoing issue. Our records indicate that this was brought to the attention of New Horizons as early as September 1990 in a meeting with the Baltimore District Office. This inspection revealed that components with expiration dates in March 1997 were pooled and that the pool was used in a product with an expiration date of June 1999, more than two years past the original expiration date. Please specify how you have or will validate this practice and the completion date for the correction of this observation.
- Regarding the temperature-monitoring device addressed in item 11 of the FDA-483, the investigators, in fact, observed that the device had not been wound and was not operating correctly. Please inform us of steps that have been taken to assure that this will not happen in the future.
- Your response about monitoring the temperature of freezers, etc. (FDA-483 item 12), does not address whether you can detect out-of-specification temperatures over night or over a weekend.
- Your response to item 14 indicates that your audits and management reviews address only pragmatic issues. Audits and management reviews must also address compliance with the regulations as they apply to your product. Please assure that future audits and reviews will address regulatory issues.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to all requirements of the Act and regulations at the Columbia, Maryland facility. The specific violations noted in this letter and in the FDA-483 issued at the closeout of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If you determine the causes to be systems problems, you must promptly initiate permanent corrective actions.

Federal agencies are advised of the issuance of all Warning Letters concerning device products so that they may take this information into account when awarding contracts. Additionally, no pre-market submissions for devices to which the QSR deficiencies are reasonably related will be cleared until the violations have been corrected. Also no requests for Certificate for Products for Export will be approved until the violations related to the subject devices have been corrected.

In order to facilitate FDA in making the determination that such corrections have been made, thereby enabling FDA to withdraw its advisory to other federal agencies concerning the award of government contracts, and to resume marketing clearance and export clearance of products manufactured at the Columbia facility, we are requesting that you submit to this office on the schedule below, certification by an outside expert consultant that he or she has conducted an audit of your firm's manufacturing and quality assurance systems relative to the requirements of the device QSR regulation (21 CFR, Part 820). You should also submit a copy of the consultant's report and certification by the firm's CEO (if other than yourself) that he or she has reviewed the consultant's report and that your firm has initiated or completed all corrections called for in the report. The enclosed guidance may be helpful in selecting an appropriate consultant.

The initial certifications of audit and corrections and subsequent certifications of updated audits and corrections should be submitted to this office by the following dates:

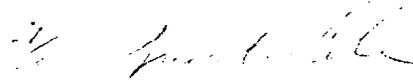
- Initial certifications by consultant and firm - August 20, 1999
- Subsequent certifications - August 18, 2000 and August 17, 2001

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

Please 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 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, Baltimore District, 900 Madison Avenue, Baltimore, Maryland 21201, to the attention of Thomas C. Knott, Compliance Officer. Mr. Knott can be reached at (410) 962-3461, extension 122.

Sincerely,



Elaine Knowles Cole
Director, Baltimore District

Enclosure