



CBER-98-023

Food and Drug Administration
Rockville MD 20857

WARNING LETTER

AUG 11 1998

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Sean Lance
President and CEO
Chiron Corporation
4560 Horton Street
Emeryville, California 94608-2916

Dear Mr. Lance:

During an inspection of your facility, located at 4560 Horton Street, Emeryville, California, from May 4 to June 5, 1998, our investigators inspected your in vitro diagnostic product and drug product operations.

In Vitro Diagnostic Products

The in vitro diagnostic products are devices as defined by Section 201(h) of the Federal Food, Drug and Cosmetic Act (the Act). Our investigators identified violations of the Act, Section 501(h), and of the Medical Device Quality System Regulations found in Title 21, Code of Federal Regulations (21 CFR), Part 820, Subchapter H, as follows:

1. Failure to develop, conduct, control and monitor production processes for handling _____ a component, to ensure the finished product in which _____ is used conforms to its specifications [21 CFR 820.70].
 - a. _____ lot MFE305, which is presently in use, was manufactured between July 1989 and August 1990. Your firm lacks data showing _____ is stable for this time period.
 - b. The controls over the _____ component have not been adequate to detect/prevent contamination. In addition, the effect of reworking has not been monitored. _____ which is not tested for bioburden, was filtered _____ times to remove bacteria, centrifuged _____ to

example, the specification for agitation of HCV [REDACTED]
the range covered by the retrospective validation was [REDACTED]

6. Failure to investigate bacterial growth on the rinsing [REDACTED] control used in bioburden testing of RIBA HCV Kit reagents in the microbiological laboratory [21 CFR 820.100(a)(2)].
7. Failure to adequately document the investigation and to identify the actions needed to correct and prevent the recurrence of [REDACTED] which were found in raw materials [REDACTED] diagnostic use only) on [REDACTED] occasions during April and May 1998 [(21 CFR 820.100(a)(2) and(3)].
8. Failure to analyze reagent log quality records, discrepancy reports, and records of initial failures to identify causes of non-conforming product, or other quality problems [21 CFR 820.100(a)(1)].
 - a. Records show the log of quality control reagents made during 1996 was reviewed during 1998. The 1998 review indicated mistakes may have been made. For example, on some occasions [REDACTED] of [REDACTED] was used to make ELISA wash buffer and on other occasions [REDACTED] were used.
 - b. SOP.#QA-087 entitled “Quality Assurance Diagnostics: Discrepancy Report and Corrective Action Report Tracking and Trending” does not address the need to take open discrepancy reports and corrective action reports into account when trending.
 - c. Initial testing failures are not tracked and trended.
9. Failure to establish and maintain procedures for receiving, reviewing, and evaluating complaints by a formally designated unit [21 CFR 820.198] in that there is no written procedure addressing the reconciliation of complaints received at Ortho Diagnostic Systems, Inc. (Ortho), distributor of your RIBA HCV 2.0 Kits, with those forwarded by Ortho to Chiron Corporation.
10. Failure to maintain complete records of complaints:
 - a. There was no record of the reply made to complainant 01647 [(21 CFR 820.198(e)(8)].
 - b. The name and address of complainant 02045 was incorrect in that some documents indicated the complainant was from [REDACTED] and others from [REDACTED] [21 CFR 820.198(e)(4)].

6. Failure to base release of components on appropriate statistical criteria [21 CFR 211.160(b)]. On two occasions, components which failed initial testing for ~~XXXXXXXXXXXX~~ were released based on retesting of a new sample. The investigation did not justify the decision to accept the passing analyses over the reject analyses.

The written response dated July 2, 1998, which addresses observations #11-47 on the Form FD-483 issued at the close of the inspection is under review. You will receive our assessment of your responses upon completion of our review. Corrective actions addressed in your previous letter may be referenced in your response to this letter, as appropriate.

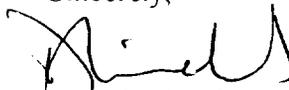
The above identified deviations are not intended to be an all inclusive list of deficiencies at your facility. It is your responsibility to assure that your facility is in compliance with all the provisions of the Federal Food, Drug and Cosmetic Act and all applicable regulations.

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.

You should notify the Food and Drug Administration 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 actions cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed. All corrective actions will be verified during reinspection of your facility. Your reply should be sent to the Food and Drug Administration, Center for Biologics Evaluation and Research, 1401 Rockville Pike, Suite 200 N, Rockville, Maryland 20852-1448, Attention: Division of Case Management, HFM-610.

Sincerely,



Daniel Michels
Acting Director
Office of Regional Operations

cc: Bernardita Mendez, Ph.D.
Vice President, Regulatory Affairs
Chiron Corporation
4560 Horton Street
Emeryville, California 94608-2916