



**CERTIFIED MAIL
RETURN RECEIPT REQUESTED**

July 8, 1998

WARNING LETTER
CIN-WL-98-54

William Sanford, President/CEO
Steris Corporation
5960 Heisley Road
Mentor, Ohio 44060

Dear Mr. Sanford:

During inspections of your firm located at the above address by the Food and Drug Administration (FDA) on September 8/October 1, 1997 and March 2/16, 1998, our Investigators determined that your firm manufactures the STERIS Biological Monitoring Kit for the STERIS PROCESS. The kit is a device as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act). The Inspection revealed that your device is 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, packaging, storage, or installation are not in conformance with the Quality System Regulation (QSR) for Medical Devices specified in Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

Failure to ensure that all quality assurance checks are appropriate and adequate for their purposes and are performed correctly.

The written test procedure for stability testing of the Biological Indicators (BIs) used in the STERIS Biological Monitoring Kit are not followed. Test procedure No. [REDACTED], "Stability Testing of BI Spore Strips" was modified on 9/4/97 to use the STERIS determined population in place of the [REDACTED] [REDACTED] stated population in all Q.A. testing calculations for "stability testing only". Your firm appears to be applying this change inconsistently without adequate explanation. For example, the STERIS determined population was used only in wash-off verification calculation at 3 and 12 months. The manufacturer's stated population is still being used for population verification calculations at 3 and 12 months as well as in preproduction wash-off verification calculations.

In addition, your firm's use of the passing criteria of "-50% to +300%" in describing the variation in population for total viable spore count is misleading. The U.S. Pharmacopeia 23 (USP 23), which your firm says it follows states: "the average number is not less than 50% of the number of viable spores of the specified strain per carrier stated on the label, and not more than 300% of that number." The phrase "+300%" used in your firm's passing criteria implies 300% greater than, or 400% of, the number.

Also, in the USP 23 the passing criteria for stability testing of BIs appear to differ from the passing criteria of "-50% to +300%" which your firm uses. For stability testing, the USP 23 states that "the average number per specimen is not less than 50% of the highest such number obtained from any previous determinations made in the same dating period." The highest number is not necessarily the number obtained during preproduction testing.

Test procedures used for quality control allow for retesting if the first test fails. For example, the SOPs for wash-off, Peracetic Acid (PA) D-value, and media acceptance allow for retesting if the first test fails. There is no scientific rationale given or documentation of an investigation of the testing procedure to show that the monitoring, materials used, testing procedure, and negative controls indicate that inadequate or faulty techniques were used in the test itself.

Failure to establish and maintain adequate process control procedures to ensure that the Biological Monitoring Kits conform to their specifications.

Your firm's stability protocol does not appear to be adequate in that it does not allow for frequent enough testing to adequately detect changes in the biological indicator (BI) spore strips over the shelf-life. For example, two lots of BIs, S53602 and S53603, exceeded specifications for D-value when tested at 12 months. These failures were dismissed by your firm since the kits containing these BI lots had expired at the time of testing. Since these lots were only tested at 3 months and 12 months, there is no way to know at what point between 3 and 12 months these lots failed.

The manufacturer's population was used in preproduction wash-off verification calculations for BI lots, S51307 and S45613. If the STERIS determined population had been used, as would be consistent with the procedure for stability wash-off verification in effect at the time, these two lots would have failed to meet specifications by having wash-off populations less than 50% of the adjusted STERIS determined population. The BI lots were accepted by your firm's QC testing.

For retrospective stability testing performed to support an 18 month expiration date for the individual BIs used in the kits, stability tests performed at the 18 months interval involved only PA D-value tests for one lot (e.g., no wash-off tests or population verification tests were performed); three out of 9 lots tested after the 18 months stability testing interval did not meet the specifications for population verification (-50% to + 300% of the STERIS determined population). The population of the BIs used for PA D-value calculations was the manufacturer's stated population not the actual population of the BI determined at the beginning of the projected expiration dating period of the lots tested.

Failure to adequately ensure that the use of nonconforming products are closely monitored and does not become accepted practice.

During your firm's current stability program which began September 1996, twenty-one (21) BI lots were undergoing stability testing. At least eight (38%) of the 21 BI spore strips in the stability testing program did not meet your firm's criteria for acceptance at preproduction testing and, according to your firm's test procedure, these lots should have been rejected and never put into kits for distribution. However, only three of these lots, S53402, S55004 and S55104, were rejected because of preproduction test results. The other out of specification BI lots were put into distribution as part of your firm's biological monitoring kits.

Three BI lots which did not meet your firm's acceptance criteria during preproduction testing, were accepted through the use of a Temporary Change Request (TCR) for D-value (lot S53603) or by conducting additional testing of criteria that failed initially (lots S53601 and S53901).

For two additional BI lots which failed to meet preproduction acceptance criteria no explanation for their acceptance and distribution was given. Lot S51907 failed preproduction wash-off verification (9.14×10^5 is 507% of the adjusted manufacturer's population). Lot S52902 failed preproduction population verification (8.0×10^5 is 320% of manufacturer's stated population).

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA 483 issued at the closeout of the FDA 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 the causes are determined to be systems problems you must promptly initiate permanent corrective actions.

Page 4
July 8, 1998

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Also, no requests for Certificates For Products For Export will be approved until the violations related to the subject devices have been corrected.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by The Food and Drug Administration without further notice. Possible actions include, but are not limited to, seizure, injunction, and/or civil penalties.

Please notify this office in writing within fifteen (15) working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within fifteen (15) working days, state the reason for the delay and the time within which the corrections will be completed.

We received your letter of response to the Form FDA 483 (List of Inspectional Observations) issued to you at the close of the FDA inspection. The actions you have taken are not adequate to correct all of the violative conditions pointed out to you (see attached FDA letter). Your letter of response has been made a permanent part of the Establishment Inspection Report of your firm.

It has come to our attention that you have made changes in procedures, specifications and acceptance criteria for your BI spore strips used in the STERIS Biological Monitoring Kit since obtaining premarket clearance. Please review the attached document "Deciding When to Submit a 510(k) for a Change to an Existing Device" to determine if a 510(k) needs to be submitted to the agency.

Your response to this Warning Letter should be sent to Evelyn D. Forney, Compliance Officer, Food and Drug Administration, 1141 Central Parkway, Cincinnati, Ohio 45202.

Sincerely,



Carol A. Heppe
Acting District Director
Cincinnati District

Attachments