



5/11/97
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Food and Drug Administration
Center for Biologics Evaluation
and Research
1401 Rockville Pike
Rockville MD 20852-1448

AUG 6 1997

WARNING LETTER

CERTIFIED
RETURN RECEIPT REQUESTED

Ms. Sandra Chin
Responsible Head
Coulter Corporation
Mail Code 31-B06
P.O. Box 169015
Miami, Florida 33116-9015

Dear Ms. Chin:

The Food and Drug Administration (FDA or the agency) conducted an inspection of Coulter Corporation, Division of Retrovirology (Coulter), 560 West 20th Street, Hialeah, Florida, from April 28-30, May 1-9, May 21 & 28, and June 3, 1997. During the inspection, our FDA investigators documented significant deviations from the applicable standards and requirements of Subchapter F, Parts 600-680, and Subchapter H, Part 820, Title 21, Code of Federal Regulations as follows:

1. Failure to adequately review, evaluate, and maintain written and oral complaints relative to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device [21 CFR 820.198(a)], in that:
 - a. Complaint report #1996070399 was closed and the corrective action section of the report was crossed out before determining the cause of the complaint.
 - b. Complaint report #1996070348 was closed while still under investigation by the customer/distributor.
2. Failure to review, evaluate, and investigate any complaint involving the possible failure of a device to meet any of its performance specifications, in that complaints #1996070351 and #1996070346 regarding instability of Antigen Reagent, were not properly investigated [21 CFR 820.198(b)].
3. Failure to maintain adequate written records of investigations, including conclusions and follow up, of failures of a device or any of its components [21 CFR 820.162]. For

example:

- a. Original complaint reports provided by the distributor are discarded and replaced with the most recent printout.
 - b. Copy of the reply to customers is not always retained in the complaint file.
 - c. Decisions and/or resolutions made during meetings between the firm and the distributors concerning complaints are not documented.
4. Failure to establish, implement, and control written manufacturing specifications and processing procedures [21 CFR 820.100], in that:
- a. Standard operating procedure (SOP) [REDACTED] entitled "[REDACTED]" was not followed regarding device failures for Antigen Reagent lots 1976J863 and 1976M993 and HIV Reaction Plates lot 1986H964 in that no investigation was conducted to determine the root cause of the failures.
 - b. SOP [REDACTED] entitled "[REDACTED]" was not followed in that purified water taps results exceeded the specified action limits and corrective actions were not initiated and/or documented. For example:
 - i. on 11-18-96 sample Tap Bank [REDACTED] resulted in 109cfu/ml exceeding the <100cfu/ml limit;
 - ii. on 2-10-97 sample Tap Water [REDACTED] resulted in 563cfu/ml exceeding the <500cfu/ml limit; and
 - iii. on 2-19-97 sample Tap Water [REDACTED] resulted TNTC exceeding the <500cfu/ml limit.
 - c. Incoming material specification for [REDACTED] plates ([REDACTED]) does not include sample size specification and references an obsolete SOP [REDACTED] entitled "General Promises and Responsibilities for Incoming Material Specifications."
 - d. QC [REDACTED] entitled "[REDACTED]" requires the collection of six HIV reaction plate samples to be tested for bioburden; however, only three samples are collected for testing.
 - e. SOP [REDACTED] entitled "[REDACTED]" does not include the procedure and corrective actions to follow when air and surface bioburden results exceed action limit specifications.
 - f. SOP [REDACTED] entitled "[REDACTED]" references an obsolete procedure [REDACTED] entitled "[REDACTED]"
5. Failure to establish, implement, and control written manufacturing specifications to assure that the device conforms to its original design or any approved changes and that such changes are subjected to controls as stringent as those applied to the original specifications

in that [REDACTED] acceptance specification for purity was changed from 98% to 96% without evaluating the effect on product performance [21 CFR 820.100(a)(2)].

6. Failure to ensure that all production and quality assurance measurement equipment, such as mechanical, automated, or electronic equipment, is suitable for its intended purposes and is capable of producing valid results [21 CFR 820.61]. For example:
 - a. The [REDACTED] pouch sealer validation does not include scientifically sound acceptance criteria and run size to demonstrate reproducibility.
 - b. The Retrovirology Laboratory balances, i.e., the [REDACTED] and the [REDACTED], are not routinely checked between calibrations.
 - c. The [REDACTED] refrigerator [REDACTED] temperature chart for November 4 through November 11, 1996, shows an out-of-specification temperature of 13°C.
7. Failure to have appropriate written procedures for acceptance of components in that the incoming material release specification for the [REDACTED] microwell strips describes the material as polypropylene; however, the certificate of analysis describes the material as crystal polystyrene [21 CFR 820.80(a)].
8. Failure to maintain a device history record to demonstrate that the device is manufactured in accordance to the device master record [21 CFR 820.184 and 600.12] in that:
 - a. The operating procedure and the equipment settings used during the April 25, 1997, re-pouching of reaction plates lot 1987D274 were not appropriately documented.
 - b. Batch production records (BPR) do not consistently indicate the reason for in-process rejects.
 - c. Corrections made to BPR for lot 1987D274 are not verified for accuracy and no reference is made to the non-conforming report.

The above violations are not intended to be an all-inclusive list of deficiencies at your establishment. In accordance with 21 CFR 600.10(a), it is your responsibility, as Responsible Head, to assure that your establishment is in compliance with all requirements of the federal regulations. Because the deficiencies described above occurred prior to the effective date (June 1, 1997) of the quality system regulations published on October 7, 1996, the citations are referenced to the regulations in effect at the time the deficiencies were noted to have occurred.

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.

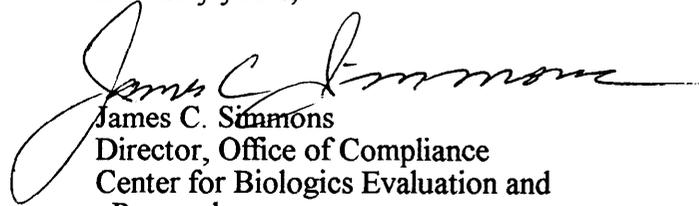
You should notify this Office in writing, within 15 working days of receipt of this letter, of specific steps you have taken to correct the noted violations and to prevent their recurrence. If

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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 my attention at the following address: Food and Drug Administration, Center for Biologics Evaluation and Research, HFM-600, Suite 200N, 1401 Rockville Pike, Rockville, Maryland 20852-1448.

Sincerely yours,



James C. Simmons
Director, Office of Compliance
Center for Biologics Evaluation and
Research