



DEPARTMENT OF HEALTH & HUMAN SERVICES

94851d
Public Health Service

Food and Drug Administration
Detroit District
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CERTIFIED MAIL
RETURN RECEIPT REQUESTED

June 17, 2004

WARNING LETTER
2004-DT-05

Dr. Attila Molnar
President and CEO
Bayer Corporation
100 Bayer Road
Pittsburgh, Pennsylvania 15205-9741

Dear Dr. Molnar:

A limited inspection of your Bayer Healthcare LLC, Mishawaka, Indiana facility was conducted from April 15 through 20, 2004. The purpose of the inspection was to evaluate the adequacy of your activities related to Recall Z-911-03; Clinitek 50 urine chemistry analyzers. Clinitek 50 urine chemistry analyzers are devices as defined by Section 201(h) of the Federal Food, Drug and Cosmetic Act (the Act). This inspection revealed that these devices are adulterated within the meaning of Section 501 of the Act, as explained further below.

The above-referenced inspection revealed that these devices are adulterated within the meaning of Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for their manufacture, packing, storage, or installation are not in conformance with the current Good Manufacturing Practice (CGMP) requirements of the Quality System regulation (QS regulation), as specified in Title 21, Code of Federal Regulations (CFR), Part 820. Significant deviations include, but are not limited to, the following:

1. Failure to establish and maintain an adequate organizational structure to ensure that your medical devices are designed and produced in accordance with the requirements of Part 820, as required by 21 CFR 820.20(b), as demonstrated by the types of observations made during these inspections. [See, for example, FDA-483 observation 5.].

2. Failure to establish and maintain a Quality System that is appropriate for the specific medical device(s) designed or manufactured, and that meets the requirements of Part 820, as required by 21 CFR 820.5. For example:
 - a. Non-conforming Clinitek 50 analyzers have been released and distributed by your Quality System. [See FDA-483 observation 1A.].
 - b. Not all Clinitek 50 analyzers that were built by an operator who had failed to install grounding straps were evaluated, inspected, or reworked to determine whether they had the same defect. [See FDA-483 observation 1A.].
 - c. Manufacturing changes were implemented without verification, validation or documentation. [See FDA-483 observation 4].
 - d. Records of re-inspection and rework activities do not exist. [See FDA-483 observation 2A.].
 - e. An untrained operator was assigned to assembly of Clinitek 50 analyzers. [See FDA-483 observations 1B.1.a. and 5c.].
 - f. There is no indication that an investigation was performed to determine whether all other employees had been properly trained to perform their assigned functions after it was determined that an untrained operator had been assigned to the assembly of Clinitek 50 analyzer. [See FDA-483 observation 1B.1.c.].
 - g. Not all corrective and preventive action activities relating to non-conforming Clinitek 50 analyzers have been documented. [See FDA-483 observation 1].

3. Failure to assure that personnel are adequately trained to perform assigned functions, as required by 21 CFR 820.25(b). For example:
 - a. An untrained operator was assigned to assemble Clinitek 50 analyzers. [See FDA-483 observation 1B.1.a. and 5c.].
 - b. Non-conforming Clinitek 50 analyzers were assembled, released and distributed without your Quality System detecting the defect. [See FDA-483 observation 1A.].
 - c. Changes to a process or procedure are not always verified or validated. [See FDA-483 observation 4].
 - d. Device acceptance activities are not always documented. [See FDA-483 observation 3].
 - e. Your CAPA documentation does not address how your controls allowed an untrained operator to be assigned to the assembly of Clinitek 50 analyzers. [See FDA-483 observation 1B.1.a.].

4. Failure to develop, conduct, control, and monitor production processes to ensure that a device conforms to its specifications, as required by 21 CFR 820.70(a). For example:
 - a. Non-conforming Clinitek 50 analyzers were manufactured, released and distributed without detection of the defect. [See FDA-483 observation 1].
 - b. A non-trained operator was assigned to assemble Clinitek 50 analyzers. [See FDA-483 observation 1B.i.a.].
 - c. Procedures were not followed for the control of Clinitek 50 analyzers that did not conform to specifications. [See FDA-483 observation 2].
5. Failure to have acceptance records for Clinitek 50 analyzers documenting the dates the acceptance activities were performed, the results, the signature of the individual(s) conducting the activities and, where appropriate the equipment used, as required by 21 CFR 820.80(e). For example, acceptance activity records could not be located for the testing of [REDACTED] [See FDA-483 observation 3].
6. Failure to establish and maintain procedures for rework, and to document product rework and reevaluation activities, in the device history record, as required by 21 CFR 820.90(b)(2). For example:
 - a. Re-inspection and rework records associated with Diagnostics Manufacturing Requisition/Order S190A were not available for review. [See FDA-483 observation 2A.].
 - b. Some rework records associated with Diagnostics Manufacturing Requisition/Order S188A do not indicate who conducted the re-inspections and/or rework activities. [See FDA-483 observation 2B.].
7. Failure to establish and maintain adequate procedures for implementing corrective and preventive action [CAPA], which include requirements for analyzing processes, work operations, quality audit reports, quality records, service records, complaints, returned product, and other sources of quality data to identify existing and potential causes of nonconforming product or other quality problems, as required by 21 CFR 820.100(a). For example:
 - a. CAPA NPT-E-2003-0075 instructs the implementation of new controls, but no written procedures were established for implementing these controls. [See FDA-483 observation 1A.ii.d.].
 - b. CAPA NPT-E-2003-0075 was not adequately implemented in that the range of products selected for inspection, rework and retest does not reflect the total time period of manufacturing the product by employee [REDACTED]. [See FDA-483 observation 1A.i.].

8. Failure to verify or validate corrective and preventive actions to ensure that such actions are effective and do not adversely affect the finished device, as required by 21 CFR 820.100(a)(4). For example: Neither CAPA NPT-E-2003-0075 nor CAPA NPT-E-2003-0050 indicate whether the corrective and preventive actions have been verified or validated to ensure that they are effective and do not adversely affect the finished devices, or whether any problems were associated with the implementation of the CAPA actions. [See FDA-483 observations 1A.ii. and 1B.ii.].
9. Failure to document the performance of all CAPA activities, and their results, as required by 21 CFR 820.100(b).
 - a. Your firm lacks documentation that the corrective actions reported to the FDA in conjunction with Recall Z-911-03 were performed.
 - b. Some of the CAPA activities reportedly performed were not documented for either CAPA NPT-E-2003-0050 or NPT-E-2003-0075. [See FDA-483 observation 1].
10. Failure to establish and maintain procedures to ensure that Device History Records (DHRs) demonstrate that devices are manufactured according to the Device Master Records and the requirements of 21 CFR Part 820, as required by 21 CFR 820.184. For example:
 - a. It is unclear whether device history record documents associated with the [REDACTED] non-conformance refer to initial acceptance tests, re-tests, or reworks. [See FDA-483 observation 1A.ii.c.].
 - b. It is unclear whether device history record documents associated with the [REDACTED] non-conformance refer to initial acceptance tests, re-tests, or reworks. [See FDA-483 observation 1B.ii.b.].

This letter is not intended to be an all inclusive review of your firm's compliance status. It is your responsibility to assure adherence to each requirement of the regulations. Other Federal agencies are advised of the issuance of all Warning Letters about medical devices so that they may take this information into account when considering the award of contracts. Additionally, pending 510(k) or PMA applications and export approval requests may not be approved until the violations are corrected.

We request that you take prompt action to correct these violations. Failure to promptly correct violations may result in enforcement action being initiated by the Food and Drug Administration without further notice. The Federal Food, Drug, and Cosmetic Act provides for the seizure of illegal products, the assessment of civil money penalties, and for injunction against the manufacturer and/or distributor of illegal products.

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Bayer Corporation
Pittsburgh, PA

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We acknowledge receipt of the May 14, 2004 letter of Mr. Wilson Ford, Vice-President, Quality Assurance, Self Test, written in response to the FDA-483. His letter addresses the very specific nature of the inspectional observations.

The response appears adequate with one exception. The response to observation 1.B.i.c., on page 9 of Attachment 1 of the letter states,

"The need and adequacy of training is routinely assessed as part of the internal audit program. We have no evidence that there are systemic training issues."

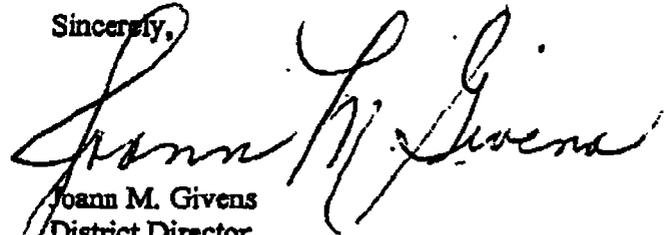
The production mistakes of two reportedly trained employees, the failure of a supervisor to properly document employee training, and the failure of your internal audit process to identify these weaknesses, suggests that there are problems requiring your attention. The management organization deficiencies cited as violation number one, the quality system deficiencies cited as violation number two, and the employee training examples listed under violation number three in this letter are indicative of the need for a thorough assessment of your complete quality system.

FDA will further evaluate the adequacy of the other elements of your response during its next inspection.

Please notify this office in writing, within fifteen (15) working days of your receipt of this letter, as to the specific steps you have taken to correct these violations. You should also include an explanation of each step being taken to identify and make corrections to assure that similar violations will not recur. If correction actions cannot be completed within 15 working days, please state the reason for the delay and the time frame within which the corrections will be implemented.

Your reply should be directed to Melvin O. Robinson, Compliance Officer, at the above address.

Sincerely,



Joann M. Givens
District Director
Detroit District

Enclosure: FDA-483