



November 24, 1997

Chicago District
300 S. Riverside Plaza, Suite 550 South
Chicago, Illinois 60606
Telephone: 312-353-5863

WARNING LETTER
CHI-5-98

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Helge H. Wehlmeier, President & CEO
Bayer Corporation (USA)
100 Bayer Road
Pittsburgh, PA 15201

Dear Mr. Wehlmeier:

During an inspection of the Kankakee, Illinois facility of the Business Group Diagnostics from August 25 to 27, 1997, Investigator Mary Kay Concannon determined your firm manufactures In-Vitro Diagnostics. In-Vitro Diagnostics are devices as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The inspection revealed the 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 manufacturing, packaging, storage, or installation are not in conformance with the Current Good Manufacturing Practice (CGMP) requirements of the Quality System Regulation, as specified in Title 21, Code of Federal Regulations (CFR), Part 820. The 1978 Good Manufacturing Practice (GMP) for Medical Device regulation was superseded on June 1, 1997, by the Quality Systems Regulation.

1. Failure to validate critical manufacturing processes. For example, the lyophilization process used in the manufacture of [redacted] Bovine Thrombin has not been validated.
2. Failure to establish process procedures that assure that [redacted] Bovine Thrombin conforms to its original design or any approved changes. Parameter ranges for critical parameters such as time, pressure and temperature are not defined in the procedure.

The inspection also revealed that the devices are misbranded within the meaning of Section 502(f)(1) of the Act, in that its labeling fails to bear adequate directions for use. The labeling of the in vitro diagnostic products includes defined expiration and storage conditions. The labeling storage requirements must be determined as specified in, 21 CFR Section 809.10 (b)(5)(iv) by reliable, meaningful, and specific test methods such as those described in 21 CFR Section 211.166. Our inspection determined that no stability testing has been performed on any of your in vitro diagnostic products for (at least) the last three years.

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This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the enclosed Form FDA 483 issued to Mr. Joseph G. Montalto, Director of Operations 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 the causes are determined to be system problems, you must promptly initiate permanent corrective actions.

We acknowledge that Mr. Montalto submitted to this office a response, dated September 10, 1997, concerning our investigator's observations noted on the Form FDA 483. We are not convinced that your response will assure that adequate correction will be taken. For example, Mr. Montalto's letter includes a commitment to perform stability testing as per SOP 301. This SOP has been in place but has not been followed. We seek assurance that the SOP would be followed.

You should take prompt action to correct any manufacturing or quality systems deviations identified by your internal audits. Failure to promptly correct these deviations may be identified in a later comprehensive follow-up inspection, and may result in regulatory action being initiated by the Food and Drug Administration without further notice.

Please notify this office in writing within 15 working days of receipt of this letter regarding the specific steps you have taken to correct the above violations, including an explanation of each step being taken to prevent the recurrence of similar violations. 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 response should be sent to Stephen Eich, Compliance Officer.

Sincerely,

/s/

Raymond V. Mlecko
District Director

Enclosure