DEPARTMENT OF HEALTH & HUMAN SERVICES

s 4452d

Food and Drug Administration
Rockville MD 20857

WARNING LETTER

VIA FEDERAL EXPRESS

Date: DEC 23 2003

Hans-ole Hedegaard
President and CEO
Eldon Biologicals A/S
10 Standtoften
Gentofte, 2820, Denmark

Dear Mr. Hedegaard,

During an inspection of your firm located in Gentofte, Denmark, by the Food and Drug Administration (FDA) on August 25, 2003 through August 27, 2003, our investigator determined that your firm manufactures the [redacted]. These products are devices as defined by section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The above-stated inspection revealed there was evidence of change in intended use and labeling of the devices to deem these [redacted] adulterated under section 501(f)(1)(B) of the Act, in that they are class III devices under section 513(f) and you do not have an approved application for premarket approval in effect pursuant to section 515(a) or an approved application for investigational device exemption under section 520(g). These devices are also misbranded under section 502(o), because a notice or other information respecting these devices was not provided to the FDA as required by section 510(k). The original submission was cleared for the intended use of [redacted] and for [redacted] but not for [redacted] Two batches/lots, [redacted], were distributed to the United States between May 30 and August 19, 2003.

The above-stated inspection also 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, the manufacture, packing, 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. Significant deviations include, but are not limited to the following:

1. Failure to establish and maintain an adequate organizational structure, review the suitability and effectiveness of the quality system by management, and establish quality system procedures and instructions, as required by 21 CFR 820.20(b), (c), and (e). For example:

a. Quality system procedures were not complete and implemented.

b. The organizational structure to include responsibilities and authorities has not been formally established.

c. Procedures for management review are not complete and implemented nor have any such reviews been conducted.

2. Failure to establish and maintain adequate procedures for implementing corrective and preventive action, as required by 21 CFR 820.100(a) and (b). For example:

a. The procedure titled Corrective Action Handling [redacted] was not approved and implemented to address corrective and preventive actions and no established procedure was found to have been in place.

b. Microsoft 2000 Excel spreadsheet software used in manufacturing has not been validated for the purpose of generating a worksheet for formulation of reagents. No documentation was found to establish or verify corrections made to the program.

c. A report dated November 11, 2002 on non-conforming material on [redacted] was filed and a possible cause for the [redacted] was given; however no documentation was provided to verify or validate the adequacy of the corrective and preventive actions.

d. Problems were recorded relating to the use of the new dosing/dispensing machine [redacted]; however no documentation/evidence was provided to verify or validate the adequacy of the corrective and preventive actions.

3. Failure to establish and maintain adequate procedures for receiving, review, and evaluation of complaints by a formally designated unit ensuring all complaints are processed in a uniform and timely manner, as required by 21 CFR 820.198. For example:

a. The procedure titled Complaint Handling [redacted] was not approved and implemented to address complaints about your product.

b. No formal complaint files were documented.

c. Complaints are not reviewed and evaluated to determine whether the complaint represents an event reportable to the FDA under Part 803, Medical Device Reporting.

4. Failure to adequately and fully validate and approve a process whose results cannot be fully verified by subsequent inspection and test, as required by 21 CFR 820.75(a). For example:

a. The [redacted] dispensing machine has not been validated to ensure the proper dispensing of reagents.

b. The drying oven has not been validated to ensure that reagents dispensed on each configuration of the cards can be dried sufficiently.

5. Failure to validate computer software for its intended use according to an established protocol, as required by 21 CFR 820.70(i). For example, the Microsoft 2000 Excel spreadsheet software program was not validated for formulation of reagents and was seen to give incorrect data.

6. Failure to establish and maintain procedures to control all documents, as required by 21 CFR 820.40. For example, changes were noted to various documents, records, procedures, specifications, and labeling but no formal procedures for review and approval were completed.

7. Failure to establish and maintain procedures to ensure that all purchased or otherwise received product and services conform to specified requirements, as required by 21 CFR 820.50. For example, the purchasing procedure has not been reviewed, approved or implemented and no previous procedure was in use.

8. Failure to have quality audits conducted by individuals who do not have direct responsibility for the matters being audited, as required by 21 CFR 820.22. For example, no internal quality audits have been conducted of your quality system.

Additionally, your devices are misbranded under section 502(t)(2) of the Act, in that your firm failed to submit information to the FDA as required by the Medical Device Reporting (MDR) regulation, as specified in 21 CFR Part 803. Specifically, you failed to implement a Medical Device Reporting (MDR) procedure. You should ensure that MDR reports are investigated and the cause of the problem is determined.

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 on the form FDA 483 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.

You should take prompt action to correct these violations. Failure to promptly correct these violations may result in regulatory action being initiated by the FDA without further notice.

Also, federal agencies are informed about the Warning Letters we issue, such as this one, so that they may consider this information when awarding government contracts.

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 15 working days, state the reason for the delay and the time within which the corrections will be completed. If documentation is not in English, please provide the English translation to facilitate our review.

Please address your response to the Food and Drug Administration, Center for Devices and Radiological Health, Office of In Vitro Diagnostics, 2098 Gaither Road, Rockville, Maryland 20850, to the attention of Tara Goldman.

Sincerely,

Steven A. Masiello
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

Steven I. Gutman, M.D., M.B.A
Director, Office of In Vitro Diagnostic
Device Evaluation and Safety
Center for Devices and Radiological Health