DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

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Spectral Diagnostics, Inc.
c/o Mr. Thomas M. Tsakeris
Devices and Diagnostics Consulting Group, Inc.
16809 Briardale Road
Rockville, MD 20855

JUN 16 2003

Regulation Number: 21 CFR § 866.3210
Classification: Class II
Product Code: NGS

Re: K021885
Evaluation of Automatic Class III Designation
Endotoxin Activity Assay

Dear Mr. Tsakeris:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your petition for classification of the Endotoxin Activity Assay that is intended to be used in conjunction with other clinical information such as clinical signs, other laboratory and/or radiographic test results to aid in the risk assessment of patients on their first day of admission to the ICU for progression to severe sepsis. Patients tested on their first day of admission to the ICU where the EAA value is ≥ 0.60 are three times more likely to develop severe sepsis within the next 24 hours than subjects whose EAA values are < 0.40. FDA concludes that this device, and substantially equivalent devices of this generic type, should be classified into class II. This order, therefore, classifies the Endotoxin Activity Assay, and substantially equivalent devices of this generic type into class II under the generic name, Endotoxin Assay. This order also identifies the special controls applicable to this type device, entitled, "Class II Special Controls Guidance Document: Endotoxin Assay".

FDA identifies this generic type of device as:

21 CFR 866.3210 Endotoxin Assay. An endotoxin assay is a device that uses serological techniques in whole blood. The device is intended for use in conjunction with other laboratory findings and clinical assessment of the patient to aid in the risk assessment of critically ill patients for progression to severe sepsis.

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In accordance with section 513(f)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360c(f)(1)) (the act), devices that were not in commercial distribution prior to May 28, 1976 (the date of enactment of the Medical Device Amendments of 1976 (the amendments)), generally referred to as postamendments devices, are classified automatically by statute into class III without any FDA rulemaking process. These devices remain in class III and require premarket approval, unless and until the device is classified or reclassified into class I or II or FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the act (21 U.S.C. 360c(i)), to a predicate device that does not require premarket approval. The agency determines whether new devices are substantially equivalent to previously marketed devices by means of premarket notification procedures in section 510(k) of the act (21 U.S.C. 360(k)) and Part 807 of the FDA regulations (21 CFR 807).

Section 513(f)(2) of the act provides that any person who submits a premarket notification under section 510(k) for a device may, within 30 days after receiving an order classifying the device in class III under section 513(f)(1), request FDA to classify the device under the criteria set forth in section 513(a)(1). FDA shall, within 60 days of receiving such a request classify the device. This classification shall be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the **Federal Register** classifying the device.

On April 14, 2003, FDA filed your petition requesting classification of the Endotoxin Activity Assay into class II, after reviewing an appeal of your not substantially equivalent decision. The petition was submitted under section 513(f)(2) of the act. In accordance with section 513(f)(1) of the act, FDA issued an order on November 8, 2002 automatically classifying the (device) in class III, because it was not within a type of device which was introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, which was subsequently reclassified into class I or class II. In order to classify the (device) into class I or II, it is necessary that the proposed class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use.

After review of the information submitted in the petition, FDA has determined that the Endotoxin Activity Assay, intended for use in conjunction with other laboratory findings and clinical assessment of the patient to aid in the risk assessment of critically ill patients for progression to severe sepsis on the first day of admission to the ICU, can be classified in class II with the establishment of special controls. FDA believes that class II special controls provide reasonable assurance of the safety and effectiveness of the device type.

There are no known *direct* risks to patient health. However, failure of the test to perform as indicated or error in interpretation of results may lead to improper patient management. A falsely low endotoxin measurement could result in a determination that the patient is at a lower risk for sepsis, which could delay appropriate treatment. A falsely high endotoxin

measurement could result in a determination that the patient is at a higher risk for sepsis, which could lead to unnecessary monitoring or potentially toxic therapy. Therefore, use of assay results to adjust a treatment regimen without consideration of other clinical factors could pose a risk. The special controls document aids the manufacturer in mitigating risk by establishing performance characteristics and appropriate labeling.

In addition to the general controls of the act, the Endotoxin Activity Assay is subject to the following special controls: "Class II Special Controls Guidance Document: Endotoxin Assay". Section 510(m) of the act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device. FDA has determined premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device and, therefore, the device is not exempt from the premarket notification requirements. Thus, persons who intend to market this device must submit to FDA a premarket notification submission containing information on the endotoxin assay they intend to market prior to marketing the device.

A notice announcing this classification order will be published in the **Federal Register**. A copy of this order and supporting documentation are on file in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852 and are available for inspection between 9 a.m. and 4 p.m., Monday through Friday.

As a result of this order, you may immediately market this device, subject to the general control provisions of the Act and the special controls identified in this order.

If you have any questions concerning this classification order, please contact Ms. Freddie Poole at 301 594 2096.

Sincerely yours,

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