K021885/A3

DUPLICATE

Request for Evaluation of Automatic Class III Designation (De Novo) for Endotoxin Activity Assay (EAA) (K021885)

2003 SEP 28 P1:51

Spectral Diagnostics, Inc.
Toronto, Ontario, Canada

2003 APR 14 P 12:56

2003P-0340

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DEVICES & DIAGNOSTICS CONSULTING GROUP, INC.

Thomas M. Tsakeris
President

Regulatory Affairs Consultants

April 14, 2003

Document Mail Center, HFZ-401
Center for Devices & Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, MD 20850

RE: Request for Evaluation of Automatic Class III Designation (de novo) for Endotoxin Activity Assay (EAA), K021885.

Dear Sir/Madam:

On behalf of Spectral Diagnostics, Inc. of Toronto, Ontario, Canada, I am requesting an Evaluation of Automatic Class III Designation under section 513(f)(2) of the Federal Food, Drug and Cosmetic Act. This request is being initiated following a November 8, 2002 letter from Steve I. Gutman, M.D., M.B.A., Director, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVDE&S), stating that the EAA was determined to be not substantially equivalent to any legally marketed predicate device and because of performance considerations thought not to support the safety and effectiveness of the device relative to stated intended use claims (see Attachment 1). Following a supervisory review proceeding under 21 CFR Part 10.75 conducted by CDRH Director, David W. Feigal, M.D., MPH, I received a letter from Dr. Feigal dated March 19, 2003 (see also Attachment I) indicating his conclusion that the EAA could qualify for review under de novo classification procedures given "careful and cautionary labeling" relating to restrictions and caveats on the use of the EAA. Specifically, Dr. Feigal requested that product labeling include:

1) A limitation statement indicating that the EAA not be used outside the intensive care unit and not at times other than the first day of intensive care unit admission;
2) Information that results of testing in patients with other conditions that may trigger elevated endotoxin levels but do not progress to sepsis; and
3) Information to show change in risk with change in endotoxin values.

Given the foregoing, this request for Evaluation of Automatic Class III Designation is being made in accordance with CDRH guidance dated February 19, 1998 entitled, **"New Section 513(f)(2) – Evaluation of Automatic Class III Designation Guidance for Industry and CDRH Staff."** According to this guidance the following information is requested:

- A coversheet clearly identifying the submission as "Request for Evaluation of Automatic Class III Designation" under 513(f)(2).

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- The 510(k) number under which the device was found not substantially equivalent.
- A statement of cross reference to the information contained in the 510(k).
- The classification being recommended under section 513 of the act.
- A discussion of the potential benefits of the device when compared to the potential or anticipated risks when the device is used as intended.
- A complete discussion of the proposed general and/or special controls to ensure reasonable assurance of the safety and effectiveness of the device, including whether the product should be exempt from premarket review under section 510(k), whether design controls should be applicable, and what special controls would allow the Agency to conclude the device was reasonably likely to be safe and effective for its intended use.
- Any clinical or preclinical data not included in the 510(k) that are relevant to the request.

The above information can be found in this submission as follows:

This letter serves as the coversheet for the requested action to evaluate Automatic Class III Designation for the Endotoxin Activity Assay (EAA), the subject of 510(k) **K021885**.

The requested classification is **Class II.**

A discussion of the potential benefits of the EAA device when compared to the potential or anticipated risks when the device is used as intended can be found in the 510(k) under section headings (3.7 Discussion of Results, page 92 of 118 and 3.8 Risks associated with use of the EAA device, page 95 of 118). In addition, a "white paper" entitled, *Use and Interpretation of the Endotoxin Activity Assay (EAA) for risk assessment of severe sepsis for patients in the Intensive Care Unit* was submitted to the OIVDE&S subsequent to receiving Dr. Gutman's "not substantial equivalence" letter. This white paper is being re-submitted as Attachment II.

Section 3.6.1 of the 510(k) presents pre-clinical data and section 3.6.2 presents clinical data for the EAA supporting use of the test for risk assessment as reflected in the following proposed indications for use:

> "The EAA test 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 in the ICU for the development of 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."

Spectral Diagnostics, Inc. believes that the EAA device should not be exempt from premarket review under section 510(k) and should be subject to design controls and other Quality System Requirements specified under 21 CFR Part 820. In addition, Spectral

Diagnostics, Inc. believes that the EAA device should be subject to special controls in the form of an FDA guidance document. Spectral Diagnostics, Inc. has included in Attachment III a proposed draft special control guidance document for consideration by FDA. The special control guidance document addresses appropriate labeling statements of indications for use, conditions for use, test limitations, as well as pre-clinical and clinical studies that should be submitted in prospective 510(k)s to support safety and effectiveness.

Included in Attachment IV is revised package insert labeling addressing the issues cited in Dr. Feigal's letter (see above).

Should you have any questions please contact me at 301-330-2076 (phone), 301-330-2568 (fax) or DDCGI@Comcast.net.

Sincerely,

Thomas M. Tsakeris
Devices & Diagnostics Consulting Group, Inc.

C.C. Spectral Diagnostics, Inc.