4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 862

[Docket No. FDA-2018-N-3694]

Medical Devices; Clinical Chemistry and Clinical Toxicology Devices; Classification of the Meprobamate Test System

AGENCY: Food and Drug Administration, HHS.

ACTION: Final order.

SUMMARY: The Food and Drug Administration (FDA or we) is classifying the meprobamate test system into class II (special controls). The special controls that apply to the device type are identified in this order and will be part of the codified language for the meprobamate test system's classification. We are taking this action because we have determined that classifying the device into class II (special controls) will provide a reasonable assurance of safety and effectiveness of the device. We believe this action will also enhance patients' access to beneficial innovative devices, in part by reducing regulatory burdens.

DATES: This order is effective **[INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]**. The classification was applicable on April 20, 2018.

FOR FURTHER INFORMATION CONTACT: Ryan Lubert, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 4545, Silver Spring, MD 20993-0002, 240-402-6357, Ryan.Lubert@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

Upon request, FDA has classified the meprobamate test system as class II (special

controls), which we have determined will provide a reasonable assurance of safety and

effectiveness. In addition, we believe this action will enhance patients' access to beneficial

innovation, in part by reducing regulatory burdens by placing the device into a lower device class

than the automatic class III assignment.

The automatic assignment of class III occurs by operation of law and without any action

by FDA, regardless of the level of risk posed by the new device. Any device that was not in

commercial distribution before May 28, 1976, is automatically classified as, and remains within,

class III and requires premarket approval unless and until FDA takes an action to classify or

reclassify the device (see 21 U.S.C. 360c(f)(1)). We refer to these devices as "postamendments

devices" because they were not in commercial distribution prior to the date of enactment of the

Medical Device Amendments of 1976, which amended the Federal Food, Drug, and Cosmetic

Act (FD&C Act).

FDA may take a variety of actions in appropriate circumstances to classify or reclassify a

device into class I or II. We may issue an order finding a new device to be substantially

equivalent under section 513(i) of the FD&C Act (21 U.S.C. 360c(i)) to a predicate device that

does not require premarket approval. We determine whether a new device is substantially

equivalent to a predicate by means of the procedures for premarket notification under section

510(k) of the FD&C Act (21 U.S.C. 360(k)) and part 807 (21 CFR part 807).

FDA may also classify a device through "De Novo" classification, a common name for

the process authorized under section 513(f)(2) of the FD&C Act. Section 207 of the Food and

Drug Administration Modernization Act of 1997 (Pub. L. 105-115) established the first procedure for De Novo classification. Section 607 of the Food and Drug Administration Safety and Innovation Act (Pub. L. 112-144) modified the De Novo application process by adding a second procedure. A device sponsor may utilize either procedure for De Novo classification.

Under the first procedure, the person submits a 510(k) for a device that has not previously been classified. After receiving an order from FDA classifying the device into class III under section 513(f)(1) of the FD&C Act, the person then requests a classification under section 513(f)(2).

Under the second procedure, rather than first submitting a 510(k) and then a request for classification, if the person determines that there is no legally marketed device upon which to base a determination of substantial equivalence, that person requests a classification under section 513(f)(2) of the FD&C Act.

Under either procedure for De Novo classification, FDA shall classify the device by written order within 120 days. The classification will be according to the criteria under section 513(a)(1) of the FD&C Act. Although the device was automatically placed within class III, the De Novo classification is considered to be the initial classification of the device.

We believe this De Novo classification will enhance patients' access to beneficial innovation, in part by reducing regulatory burdens. When FDA classifies a device into class I or II via the De Novo process, the device can serve as a predicate for future devices of that type, including for 510(k)s (see 21 U.S.C. 360c(f)(2)(B)(i)). As a result, other device sponsors do not have to submit a De Novo request or premarket approval application to market a substantially equivalent device (see 21 U.S.C. 360c(i), defining "substantial equivalence"). Instead, sponsors can use the less-burdensome 510(k) process, when necessary, to market their device.

II. De Novo Classification

On February 21, 2017, Lin-Zhi International, Inc. submitted a request for De Novo classification of the LZI Carisoprodol Metabolite (Meprobamate) Enzyme Immunoassay. FDA reviewed the request in order to classify the device under the criteria for classification set forth in section 513(a)(1) of the FD&C Act.

We classify devices into class II if general controls by themselves are insufficient to provide reasonable assurance of safety and effectiveness, but there is sufficient information to establish special controls that, in combination with the general controls, provide reasonable assurance of the safety and effectiveness of the device for its intended use (see 21 U.S.C. 360c(a)(1)(B)). After review of the information submitted in the request, we determined that the device can be classified into class II with the establishment of special controls. FDA has determined that these special controls, in addition to the general controls, will provide reasonable assurance of the safety and effectiveness of the device.

Therefore, on April 20, 2018, FDA issued an order to the requester classifying the device into class II. FDA is codifying the classification of the device by adding 21 CFR 862.3590. We have named the generic type of device meprobamate test system, and it is identified as a device intended to measure meprobamate in human specimens. Measurements obtained by this device are used to detect the presence of meprobamate to diagnose the use or overdose of meprobamate or structurally-related drug compounds (e.g., prodrugs).

FDA has identified the following risks to health associated specifically with this type of device and the measures required to mitigate these risks in table 1.

Table 1.--Meprobamate Test System Risks and Mitigation Measures

Identified Risks	Mitigation Measures
Clinical action based on incorrect test results (false positive results, false negative results) may lead to inappropriate clinical decision making	Special controls (1) (21 CFR 862.3590(b)(1)), (2) (21 CFR 862.3590(b)(2)), and (3) (21 CFR 862.3590(b)(3))
Incorrect understanding of the device and test system and results may lead to inappropriate clinical decision making	Special controls (2) (21 CFR 862.3590(b)(2)) and (3) (21 CFR 862.3590(b)(3))

FDA has determined that special controls, in combination with the general controls, address these risks to health and provide reasonable assurance of safety and effectiveness. For a device to fall within this classification, and thus avoid automatic classification in class III, it would have to comply with the special controls named in this final order. The necessary special controls appear in the regulation codified by this order. This device is subject to premarket notification requirements under section 510(k) of the FD&C Act.

At the time of classification, meprobamate test systems are for prescription use only.

III. Analysis of Environmental Impact

We have determined under 21 CFR 25.34(b) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

IV. Paperwork Reduction Act of 1995

This final order establishes special controls that refer to previously approved collections of information found in other FDA regulations and guidance. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in the guidance document "De Novo Classification Process (Evaluation of Automatic Class III Designation)" have been approved under OMB control number 0910-0844; the collections of information in 21

CFR part 814, subparts A through E, regarding premarket approval, have been approved under OMB control number 0910-0231; the collections of information in part 807, subpart E, regarding premarket notification submissions, have been approved under OMB control number 0910-0120; the collections of information in 21 CFR part 820, regarding quality system regulations, have been approved under OMB control number 0910-0073; and the collections of information in 21 CFR parts 801 and 809, regarding labeling, have been approved under OMB control number 0910-0485.

List of Subjects in 21 CFR Part 862

Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 862 is amended as follows:

PART 862-- CLINICAL CHEMISTRY AND CLINICAL TOXICOLOGY DEVICES

1. The authority citation for part 862 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 360*l*, 371.

2. Add § 862.3590 to subpart D to read as follows:

§ 862.3590 Meprobamate test system.

(a) *Identification.* A meprobamate test system is a device intended to measure meprobamate in human specimens. Measurements obtained by this device are used to detect the presence of meprobamate to diagnose the use or overdose of meprobamate or structurally-related drug compounds (e.g., prodrugs).

(b) *Classification.* Class II (special controls). The special controls for this device are:

(1) Design verification and validation must include:

(i) Robust data demonstrating the accuracy of the device when used in the intended specimen matrix. The accuracy data must include a comparison between the meprobamate test system results and meprobamate results that are measured on an FDA-accepted measurement method that is specific and accurate (e.g., gas or liquid chromatography combined with tandem mass spectrometry).

(ii) Robust analytical data demonstrating the performance characteristics of the device, including, but not limited to, specificity, cross-reactivity to relevant endogenous and exogenous substances, and the reproducibility of analyte detection around the cutoff(s).

(2) The intended use of the device must not include an indication for use in monitoring therapeutic drug concentrations or informing dosing adjustment decisions.

(3) Your 21 CFR 809.10 labeling must include the following:

(i) If indicated for use as a screening test to identify preliminary results for further confirmation, the intended use must state "This assay provides only a preliminary analytical result. A more specific alternative chemical confirmatory method (e.g., gas or liquid chromatography and mass spectrometry) must be used to obtain a confirmed analytical result. Clinical consideration and professional judgment must be exercised with any drug of abuse test, particularly when the preliminary test result is positive."

(ii) A limiting statement that reads as follows: "This test should not be used to monitor therapeutic drug concentrations or to inform dosing adjustment decisions."

Dated: October 29, 2018.

Leslie Kux,

Associate Commissioner for Policy.

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