DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098
Rockville MD 20850

Alan Coley
Vice President - Operations
Tm Bioscience Corporation
439 University Ave., Suite 900
Toronto, Ontario M5G 1Y8

Re: k043011, Evaluation of Automatic Class III Designation
Tag-It™ Cystic Fibrosis Kit
Regulation Number: 21 CFR 866.5900
Classification: Class II
Product Code: NUA

MAY - 9 2005

Dear Mr. Coley:

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 Tag-It™ Cystic Fibrosis Kit. The Tag-It™ Cystic Fibrosis Kit is a device used to simultaneously detect and identify a panel of mutations and variants in the cystic fibrosis transmembrane conductance regulator (CFTR) gene in human blood specimens. The panel includes mutations and variants currently recommended by the American College of Medical Genetics and American College of Obstetricians and Gynecologists (ACMG/ACOG), plus some of the worlds most common and North American-prevalent mutations. The Tag-It™ Cystic Fibrosis Kit is a qualitative genotyping test which provides information intended to be used for carrier testing in adults of reproductive age, as an aid in newborn screening, and in confirmatory diagnostic testing in newborns and children. The kit is not indicated for use in fetal diagnostic or pre-implantation testing. This kit is also not indicated for stand-alone diagnostic purposes.

FDA concludes that this device, and substantially equivalent devices of this generic type, should be classified into class II. This order, therefore, classifies the Tag-It™ Cystic Fibrosis Kit, and substantially equivalent devices of this generic type into class II under the generic name, Cystic fibrosis transmembrane conductance regulator (CFTR) gene mutation detection system. This order also identifies the special controls applicable to this device.

FDA identifies this generic type of device as:

21 CFR 866.5900 Cystic fibrosis transmembrane conductance regulator (CFTR) gene mutation detection system. The CFTR gene mutation detection system is a device used to simultaneously detect and identify a panel of mutations and variants in the CFTR gene. It is intended as an aid in confirmatory diagnostic testing of individuals with suspected cystic fibrosis (CF), carrier identification, and newborn screening. This device is not intended for stand-alone diagnostic purposes, prenatal diagnostic, pre-implantation or population screening.

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 type. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the **Federal Register** classifying the device type.

On April 5,2005, FDA filed your petition requesting classification of the Tag-It™ Cystic Fibrosis Kit into class II. 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 April 1, 2005, automatically classifying the Tag-It™ Cystic Fibrosis Kit 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 Tag-It™ Cystic Fibrosis Kit 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 Tag-It™ Cystic Fibrosis Kit, intended to:

> "simultaneously detect and identify a panel of mutations and variants in the cystic fibrosis transmembrane conductance regulator (CFTR) gene in human blood specimens. The panel includes mutations and variants currently recommended by the American College of Medical Genetics and American College of Obstetricians and Gynecologists (ACMG/ACOG), plus some of the worlds most common and North American-prevalent mutations. The Tag-It™ Cystic Fibrosis Kit is a qualitative genotyping test which provides information intended to be used for carrier testing in adults of reproductive age, as an aid in newborn screening, and in confirmatory diagnostic testing in newborns and children. The kit is not indicated for use in fetal diagnostic or pre-implantation testing. This kit is also not indicated for stand-alone diagnostic purposes."

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.

FDA has identified no direct risks to health related to use of CFTR gene mutation detection system. However, failure of the CFTR mutation detection system to perform as indicated or errors in interpretation of results may lead to improper clinical recommendations and medical patient management. In the context of carrier-screening in adults, a false-negative or false-positive interpretation could lead to inaccurate estimates of a couple's risk of having a child with cystic fibrosis. In the context of assisting in the diagnosis of CF in newborns and confirmatory diagnostic testing of individuals with suspected CF, a false-negative could lead to a delay in the definitive diagnosis and treatment; a false-positive interpretation could lead to unnecessary or inappropriate treatment.

The measures FDA recommends to mitigate these risks are described in the guidance document, "Class II Special Controls Guidance Document: CFTR Gene Mutation Detection Systems", which includes recommendations for performance validation and labeling.

In addition to the general controls of the act, CFTR gene mutation detection systems are subject to the following special controls: "Class II Special Controls Guidance Document: CFTR Gene Mutation Detection Systems". 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 CFTR gene mutation detection system 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 Zivana Tezak at (240) 276-0597.

Sincerely yours,

Steven Gutman

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