

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 866

[Docket No. 2007N-0294]

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Certifier Reese

Medical Devices: Immunology and Microbiology Devices: Classification of In Vitro Human Immunodeficiency Virus Drug Resistance Genotype Assay

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is classifying an in vitro human immunodeficiency virus (HIV) drug resistance genotype assay into class II (special controls). The special control that will apply to this device is the guidance document entitled "Class II Special Controls Guidance Document: In Vitro HIV Drug Resistance Genotype Assay." FDA is classifying the device into class II (special controls) in order to provide a reasonable assurance of safety and effectiveness of this device. Elsewhere in this issue of the **Federal Register**, FDA is announcing the availability of the guidance document that will serve as the special control for this device.

DATES: This rule becomes effective [*insert date 30 days after date of publication in the Federal Register*]. The classification of this device into class II became effective on September 26, 2001.

FOR FURTHER INFORMATION CONTACT: Nathaniel L. Geary, Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, MD 20852, 301-827-6210.

SUPPLEMENTARY INFORMATION:

I. Background

In accordance with section 513(f)(1) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360c(f)(1)), devices that were not in commercial distribution before May 28, 1976, the date of enactment of the Medical Device Amendments of 1976, 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, to a predicate device that does not require premarket approval. FDA determines whether new devices are substantially equivalent to predicate devices by means of premarket notification procedures in section 510(k) of the act (21 U.S.C. 360(k)) and part 807 (21 CFR part 807) of FDA's regulations.

Section 513(f)(2) of the act provides that any person who submits a premarket notification under section 510(k) of the act for a device that has not previously been classified may, within 30 days after receiving an order classifying the device in class III under section 513(f)(1) of the act, request FDA to classify the device under the criteria set forth in section 513(a)(1) of the act. FDA shall, within 60 days of receiving such a request, classify the device by written order. This classification shall be the initial classification of the device.

In accordance with section 513(f)(1) of the act, FDA issued an order on June 27, 2001, classifying into class III the Visible Genetics, Inc., TRUEGENE HIV Genotyping Kit and OpenGene DNA Sequencing System, because this device was not substantially equivalent to a device that was introduced or

delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, or to a device which was subsequently reclassified into class I or class II. On July 11, 2001, Visible Genetics, Inc. submitted to FDA a petition requesting classification of the TRUEGENE HIV Genotyping Kit and OpenGene DNA Sequencing System under section 513(f)(2) of the act. The manufacturer recommended that the device be classified into class II (Ref. 1).

In accordance with section 513(f)(2) of the act, FDA reviewed the petition in order to classify the device under the criteria for classification set forth in section 513(a)(1) of the act. Devices are to be classified 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 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 determined that the Visible Genetics, Inc., TRUEGENE HIV Genotyping Kit and OpenGene DNA Sequencing System can be classified in class II with the establishment of special controls. FDA believes that special controls, in addition to general controls, are adequate to provide reasonable assurance of the safety and effectiveness of this device and that there is sufficient information to establish special controls to provide such assurance.

This device is assigned the generic name, "In vitro HIV drug resistance genotype assay." It is identified as an in vitro diagnostic device to be used to detect HIV genomic mutations that confer resistance to specific types of antiretroviral drugs, as an aid in monitoring and treating HIV infection.

FDA has identified the risks to health associated with the use of the in vitro HIV drug resistance genotype assay. These risks include inaccurate detection of resistance mutations present in a patient's viral swarm that can

result in continuance of therapies that are no longer appropriate, or changes to new, inadequate therapies. In both cases, the patient's viral load may increase, worsening the clinical prognosis and accelerating the development of drug resistant viruses. Patients may be needlessly subjected to serious, deleterious side effects of inappropriate antiviral drugs. Furthermore, failure of the assay to give any results at all (sequence failure) can deny or delay beneficial, appropriate therapies, which may also result in high viral loads and their attendant morbidity.

FDA believes that the class II special controls guidance document will aid in mitigating the potential risks to health by providing recommendations on performance characteristics; other considerations such as design controls, statistical methods, and instruments and software; product modification; and labeling. The guidance document also provides recommendations for fulfilling the premarket (510(k)) submission requirements for this device. FDA believes that the class II special controls guidance document, in addition to general controls, addresses the risks to health identified in the previous paragraph and provides reasonable assurance of the safety and effectiveness of the in vitro HIV drug resistance assay. Therefore, on September 26, 2001, FDA issued an order to the petitioner classifying the device into class II. FDA is codifying this device classification at 21 CFR 866.3950.

Following the effective date of this final classification rule, manufacturers submitting a 510(k) premarket notification for an in vitro HIV drug resistance genotype assay will need to address the issues covered in the special controls guidance. However, the manufacturer need only show that its device meets the recommendations of the guidance or in some other way provides equivalent assurance of safety and effectiveness.

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 that premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of this type of device and, therefore, this type of device is not exempt from premarket notification requirements. Persons who intend to market this type of device must submit to FDA a premarket notification, before marketing the device, which contains information about the in vitro HIV drug resistance genotype assay they intend to market.

II. Analysis of Impacts

FDA has examined the impacts of the final rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104-4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this final rule is not a significant regulatory action under the Executive order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because classification of this device into class II will relieve manufacturers of the device of the cost of complying with the premarket approval requirements of section 515 of the act (21 U.S.C. 360e), and may permit small

potential competitors to enter the marketplace by lowering their costs, the agency certifies that the final rule will not have a significant impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing "any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100,000,000 or more (adjusted annually for inflation) in any one year." The current threshold after adjustment for inflation is \$122 million, using the most current (2005) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this final rule to result in any 1-year expenditure that would meet or exceed this amount

III. Environmental Impact

The agency has 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. Federalism

FDA has analyzed this final rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, the agency has concluded that the rule does not contain policies that have federalism implications as defined in the Executive order and, consequently, a federalism summary impact statement is not required.

V. Paperwork Reduction Act of 1995

This final rule contains no collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act (PRA) of 1995 is not required. Elsewhere in this issue of the **Federal Register**, FDA is publishing a notice announcing the availability of the guidance document entitled "Class II Special Controls Guidance Document: In Vitro HIV Drug Resistance Genotype Assay." FDA concludes that the special controls guidance document contains information collection provisions that are subject to review by the OMB under the PRA and that have been approved by OMB in accordance with the PRA under the regulations governing premarket notification submissions (part 807, subpart E, OMB control number 0910-0120).

VI. References

The following reference has been placed on display in the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Petition from Visible Genetics, Inc., dated July 11, 2001.

List of Subjects in 21 CFR Part 866

Biologics, Laboratories, 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 866 is amended as follows:

PART 866—IMMUNOLOGY AND MICROBIOLOGY DEVICES

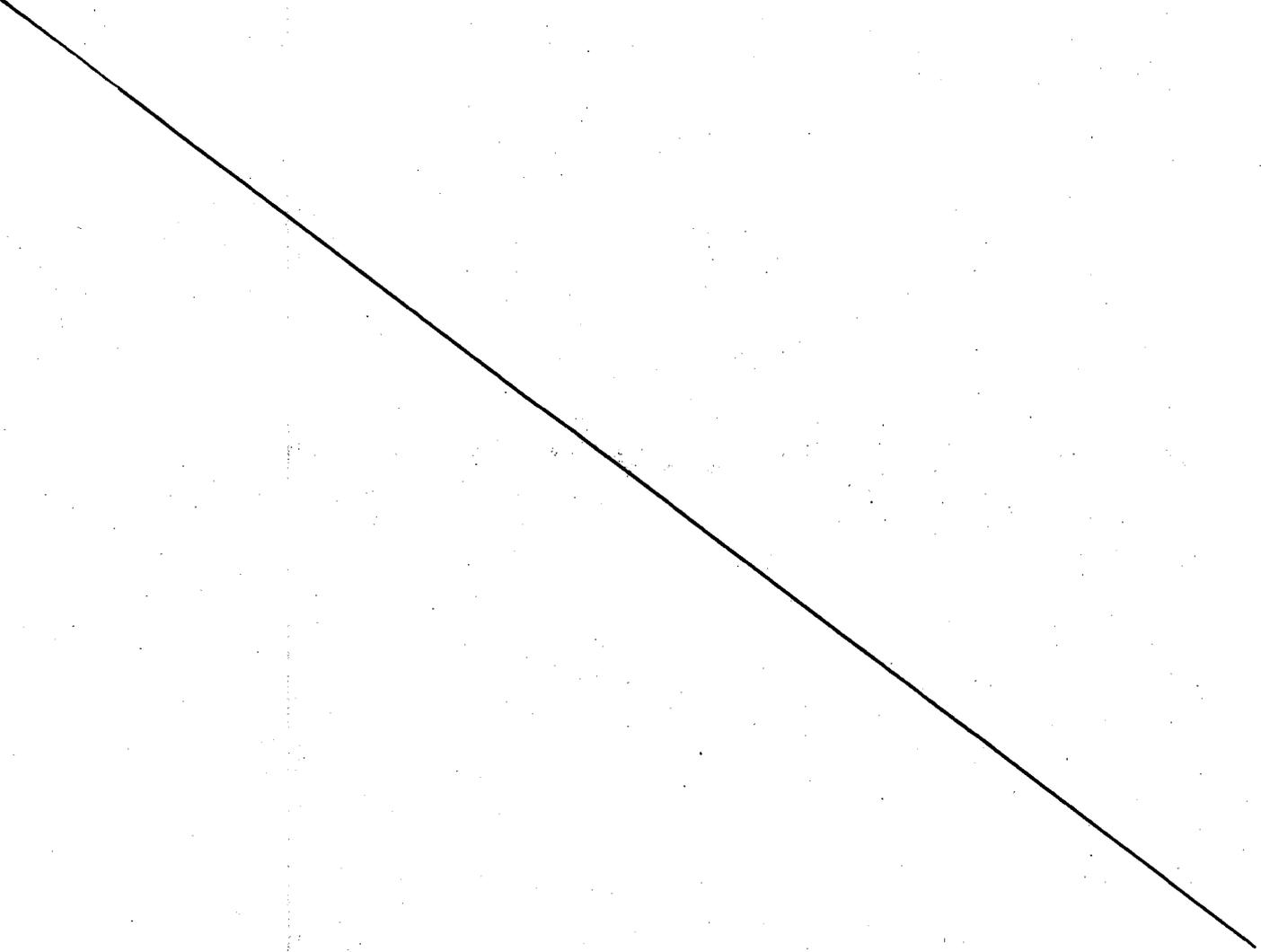
- 1. The authority citation for 21 CFR part 866 continues to read as follows:

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

■ 2. Add § 866.3950 to subpart D to read as follows:

§ 866.3950 In vitro human immunodeficiency virus (HIV) drug resistance genotype assay.

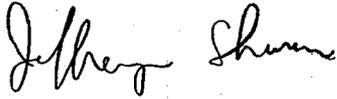
(a) *Identification.* The in vitro HIV drug resistance genotype assay is a device that consists of nucleic acid reagent primers and probes together with software for predicting drug resistance/susceptibility based on results obtained with these primers and probes. It is intended for use in detecting HIV genomic mutations that confer resistance to specific antiretroviral drugs, as an aid in monitoring and treating HIV infection.



(b) *Classification*. Class II (special controls). The special control for this device is FDA's guidance document entitled "Class II Special Controls Guidance Document: In Vitro HIV Drug Resistance Genotype Assay." See § 866.1(e) for the availability of this guidance document.

Dated: 8/2/07

August 2, 2007.



Jeffrey Shuren,
Assistant Commissioner for Policy.

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