

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

**21 CFR Part 866**

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Certifier L. CLAWSON

*DM*

[Docket No. 2005N-0471]

**Microbiology Devices; Reclassification of Herpes Simplex Virus Types 1 and 2 Serological Assays**

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Final rule.

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**SUMMARY:** The Food and Drug Administration (FDA) is reclassifying herpes simplex virus (HSV) types 1 and/or 2 (HSV 1 and 2) serological assays from class III (premarket approval) to class II (special controls). FDA had earlier proposed this reclassification on its own initiative based on new information. Elsewhere in this issue of the **Federal Register**, FDA is announcing the availability of a class II special controls guidance entitled "Class II Special Controls Guidance Document: Herpes Simplex Virus Types 1 and 2 Serological Assays."

**DATES:** This rule is effective [*insert date 30 days after date of publication in the Federal Register*].

**FOR FURTHER INFORMATION CONTACT:** Sally Hojvat, Center for Devices and Radiological Health (HFZ-440), Food and Drug Administration, 2098 Gaither Rd., Rockville, MD 20850, 240-276-0496.

**SUPPLEMENTARY INFORMATION:**

*Ch073 2005N.0471*

*NFR1*

## **I. Background**

### *A. Regulatory Authorities*

The Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 301 *et seq.*), as amended by the Medical Device Amendments of 1976 (the 1976 amendments) (Public Law 94–295), the Safe Medical Devices Act of 1990 (SMDA) (Public Law 101–629), the Food and Drug Administration Modernization Act of 1997 (FDAMA) (Public Law 105–115), and the Medical Device User Fee and Modernization Act (Public Law 107–250), established a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the act (21 U.S.C. 360c) established three categories (classes) of devices, defined by the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three categories of devices are class I (general controls), class II (special controls), and class III (premarket approval).

Under the 1976 amendments, class II devices were defined as devices for which there was insufficient information to show that general controls themselves would provide reasonable assurance of safety and effectiveness, but for which there was sufficient information to establish performance standards to provide such assurance. SMDA broadened the definition of class II devices to mean those devices for which the general controls by themselves are insufficient to provide reasonable assurance of safety and effectiveness, but for which there is sufficient information to establish special controls to provide such assurance, including performance standards, postmarket surveillance, patient registries, development and dissemination of guidelines, recommendations, and any other appropriate actions the agency deems necessary (section 513(a)(1)(B) of the act).

Under section 513 of the act, FDA refers to devices that were in commercial distribution before May 28, 1976 (the date of enactment of the 1976 amendments), as preamendments devices. FDA classifies these devices after it takes the following steps: (1) Receives a recommendation from a device classification panel (an FDA advisory committee); (2) publishes the panel's recommendation for comment, along with a proposed regulation classifying the device; and (3) publishes a final regulation classifying the device. FDA has classified most preamendments devices under these procedures. A person may market a preamendments device that has been classified into class III through premarket notification procedures, without submission of a premarket approval application (PMA), until FDA issues a final regulation under section 515(b) of the act (21 U.S.C. 360e(b)) requiring premarket approval.

Devices that were not in commercial distribution before May 28, 1976, generally referred to as postamendments devices, are classified automatically by statute (section 513(f) of the act) into class III without any FDA rulemaking process. Those devices remain in class III and require premarket approval unless and until FDA does the following: (1) Reclassifies the device into class I or II; (2) issues an order classifying the device into class I or II in accordance with section 513(f)(2) of the act, as amended by FDAMA; or (3) issues an order finding the device to be substantially equivalent, under section 513(i) of the act, to a legally marketed device that has been classified into class I or class II. The agency determines whether new devices are substantially equivalent to a legally marketed device by means of premarket notification procedures in section 510(k) of the act (21 U.S.C. 360(k)) and 21 CFR part 807.

Section 513(e) of the act governs reclassification of classified devices. This section provides that FDA may, by rulemaking, reclassify a device based upon

“new information.” FDA can initiate a reclassification under section 513(e) of the act or an interested person may petition FDA to reclassify a preamendments device. The term “new information,” as used in section 513(e) of the act, includes information developed as a result of a reevaluation of the data before the agency when the device was originally classified, as well as information not presented, not available, or not developed at that time (see, e.g., *Holland Rantos v. United States Department of Health, Education, and Welfare*, 587 F.2d 1173, 1174 n.1 (D.C. Cir. 1978); *Upjohn v. Finch*, 422 F.2d 944 (6th Cir. 1970); *Bell v. Goddard*, 366 F.2d 177 (7th Cir. 1966)).

Reevaluation of the data previously before the agency is an appropriate basis for subsequent regulatory action where the reevaluation is made in light of newly available regulatory authority (see *Bell v. Goddard*, supra, 366 F.2d at 181; *Ethicon, Inc. v. FDA*, 762 F.Supp. 382, 389–91 (D.D.C. 1991)), or in light of changes in “medical science” (see *Upjohn v. Finch*, supra, 422 F.2d at 951). Whether data before the agency are past or new, the “new information” to support reclassification under section 513(e) of the act must be “valid scientific evidence,” as defined in section 513(a)(3) of the act and 21 CFR 860.7(c)(2) (see, e.g., *General Medical Co. v. FDA*, 770 F.2d 214 (D.C. Cir. 1985); *Contact Lens Assoc. v. FDA*, 766 F.2d 592 (D.C. Cir.), cert. denied, 474 U.S. 1062 (1985)).

FDA relies upon valid scientific evidence in the classification process to determine the level of regulation for devices. To be considered in the reclassification process, the valid scientific evidence upon which the agency relies must be publicly available. Publicly available information excludes trade secret and/or confidential commercial information, e.g., the contents of a pending PMA (see section 520(c) of the act (21 U.S.C. 360j(c))).

FDAMA added section 510(m) to the act that provides that a class II device may be exempted from the premarket notification requirements under section 510(k) of the act if the agency determines that premarket notification is not necessary to assure the safety and effectiveness of the device.

### *B. Regulatory History of the Device*

In the **Federal Register** of January 9, 2006 (71 FR 1399), FDA published a proposed rule to reclassify HSV 1 and 2 serological assays into class II. These assays are used as an aid in the clinical laboratory diagnosis of diseases caused by HSV 1 and 2. FDA identified the draft guidance document entitled “Class II Special Controls Guidance Document: Herpes Simplex Virus Types 1 and 2 Serological Assays” as the special control. Interested persons were invited to comment on the proposed rule by April 10, 2006 (the draft guidance was announced in the **Federal Register** of January 9, 2006 (71 FR 1432)). A proposed rule correcting the reference section of the January 9, 2006, proposed rule was published on March 13, 2006 (71 FR 12653). FDA received no comments on the proposed reclassification.

### **II. FDA’s Conclusions**

Based on the information discussed in the preamble to the proposed rule (71 FR 1399), FDA concludes that special controls, in conjunction with general controls, provide reasonable assurance of the safety and effectiveness of these devices. Elsewhere in this issue of the **Federal Register**, FDA is announcing the availability of the special controls guidance document. Following the effective date of this final classification rule, any firm submitting a 510(k) premarket notification for a HSV 1 and 2 serological assay will need to address the issues covered in the special control guidance. However, the firm need

only show that its device meets the recommendations of the guidance or in some other way provides equivalent assurances of safety and effectiveness.

FDA is now codifying the classification and the special control guidance document for HSV 1 and 2 serological assays by amending § 866.3305 (21 CFR 866.3305). As stated in the proposed rule, FDA considered HSV 1 and 2 serological assays in accordance with section 510(m) of the act and determined that the device does need premarket notification to assure the safety and effectiveness of HSV 1 and 2 serological assays.

As stated in the preamble to the proposed rule (71 FR 1399), HSV serological assays of types other than type 1 and 2 will remain in class III. HSV nucleic acid amplification assays are not within the device type classified in § 866.3305.

### **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. Analysis of Impacts**

FDA has examined the impacts of the final rule under Executive Order 12866, and the Regulatory Flexibility Act (Public Law 96–354) (as amended by subtitle D of the Small Business Regulatory Fairness Act of 1996 (Public Law 104–121), 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

consistent with the regulatory philosophy and principles identified in the Executive order. In addition, the final rule is not a significant regulatory action as defined by the Executive order and so is not subject to review 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. Reclassification of HSV 1 and 2 serological assays from class III to class II will relieve manufacturers of the cost of complying with the premarket approval requirements in section 515 of the act. Furthermore, the special controls guidance document does not impose any new burdens on manufacturers; it advises manufacturers about ways to comply with the special controls that allow the agency to down classify these devices. By eliminating the need for premarket approval applications, reclassification will reduce regulatory costs with respect to these devices, impose no significant economic impact on any small entities, and may permit small potential competitors to enter the marketplace by lowering their costs. The agency therefore certifies that this final rule will not have a significant economic 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.

## V. 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.

## VI. Paperwork Reduction Act of 1995

FDA concludes that this final rule contains no new collections of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 is not required.

## List of Subjects in 21 CFR Part 866

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. Section 866.3305 is <sup>revised</sup> ~~amended~~ to read as follows:

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**§ 866.3305 Herpes simplex virus serological assays.**

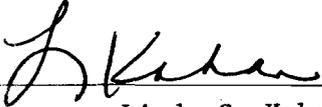
(a) *Identification.* Herpes simplex virus serological assays are devices that consist of antigens and antisera used in various serological tests to identify antibodies to herpes simplex virus in serum. Additionally, some of the assays consist of herpes simplex virus antisera conjugated with a fluorescent dye (immunofluorescent assays) used to identify herpes simplex virus directly from clinical specimens or tissue culture isolates derived from clinical specimens. The identification aids in the diagnosis of diseases caused by herpes simplex viruses and provides epidemiological information on these diseases. Herpes simplex viral infections range from common and mild lesions of the skin and mucous membranes to a severe form of encephalitis (inflammation of the brain). Neonatal herpes virus infections range from a mild infection to a severe generalized disease with a fatal outcome.

(b) *Classification.* (1) *Class II (special controls).* The device is classified as class II (special controls) if the herpes simplex virus serological assay is type 1 and/or 2. The special control for the device is FDA's guidance document entitled "Class II Special Controls Guidance Document: Herpes Simplex Virus Types 1 and 2 Serological Assays." For availability of the guidance document, see § 866.1(e).

(2) *Class III (premarket approval).* The device is classified as class III if the herpes simplex virus serological assay is a type other than type 1 and/or 2.

(c) *Date PMA or notice of completion of a PDP is required.* No effective date has been established for the requirement for premarket approval for the devices described in paragraph (b)(2) of this section. See § 866.3.

Dated: 3/23/07  
March 23, 2007.



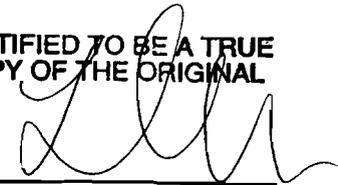
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Linda S. Kahan,  
Deputy Director,  
Center for Devices and Radiological Health.

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