

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 862

DMB

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[Docket Nos. 01P-0119 and 01P-0235]

Clinical Chemistry and Clinical Toxicology Devices; Reclassification of Cyclosporine and Tacrolimus Assays

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is reclassifying cyclosporine and tacrolimus assays from class III (premarket approval) to class II (special controls). These assays are used as an aid in the management of transplant patients receiving these drugs. FDA is also identifying the guidance document entitled "Class II Special Controls Guidance Document: Cyclosporine and Tacrolimus Assays; Guidance for Industry and FDA" as the special control the agency believes will reasonably ensure the safety and effectiveness of these devices. This reclassification is being taken after a review of petitions submitted by Dade Behring, Inc., and Microgenics, Inc. The agency is taking this action under the Federal Food, Drug, and Cosmetic Act (the act), as amended by the Medical Device Amendments of 1976 (the 1976 amendments), the Safe Medical Devices Act of 1990 (the SMDA), and the Food and Drug Administration Modernization Act of 1997 (FDAMA). 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: Cyclosporine and Tacrolimus Assays; Guidance for Industry and FDA.”

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

FOR FURTHER INFORMATION CONTACT: Jean M. Cooper, Center for Devices and Radiological Health (HFZ-440), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD, 20850, 301-594-1243.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of February 21, 2002 (67 FR 7982), FDA published a proposed rule to reclassify cyclosporine and tacrolimus assays after reviewing information contained in reclassification petitions submitted by Dade Behring, Inc., and Microgenics, Inc. FDA identified the guidance document entitled “Class II Special Controls Guidance Document: Cyclosporine and Tacrolimus Assays; Draft Guidance for Industry and FDA” as the special control capable of providing reasonable assurance of safety and effectiveness for these devices. These assays are used as an aid in the management of transplant patients receiving these drugs. Interested persons were invited to comment on the proposed rule by April 22, 2002. FDA received two comments that were supportive of its proposed reclassification, but the comments suggested specific recommendations for changes to the guidance.

II. FDA’s Conclusions

Based on a review of the available information referenced in the preamble to the proposed rule and placed on file in FDA’s Dockets Management Branch, FDA concludes that the 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 guidance document. The guidance document was revised to reflect consideration of the comments received. Following the effective date of this final classification rule, any firm submitting a 510(k) premarket notification for a cyclosporine or tacrolimus test system 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 cyclosporine and tacrolimus test systems by adding new §§ 862.1235 and 862.1678. For the convenience of the reader, FDA is also adding a new § 862.1(d) to inform the reader where to find guidance documents referenced in part 862.

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 cyclosporine and tacrolimus 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. In addition, this final rule will not impose costs of \$100 million or more on either the private sector or State, local, and tribal governments in the aggregate, and therefore a summary statement of analysis under section 202(a) of the Unfunded Mandates Reform Act of 1995 is not required.

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 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 21 CFR part 862 continues to read as follows:

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

2. Section 862.1 is amended by adding new paragraph (d) to read as follows:

§ 862.1 Scope.

* * * * *

(d) Guidance documents referenced in this part are available on the Internet at <http://www.fda.gov/cdrh/guidance.html>.

3. Section 862.1235 is added to subpart B to read as follows:

§ 862.1235 Cyclosporine test system.

(a) *Identification.* A cyclosporine test system is a device intended to quantitatively determine cyclosporine concentrations as an aid in the management of transplant patients receiving therapy with this drug. This generic type of device includes immunoassays and chromatographic assays for cyclosporine.

(b) *Classification.* Class II (special controls). The special control is "Class II Special Controls Guidance Document: Cyclosporine and Tacrolimus Assays; Guidance for Industry and FDA." See § 862.1(d) for the availability of this guidance document.

4. Section 862.1678 is added to subpart B to read as follows:

§ 862.1678 Tacrolimus test system.

(a) *Identification.* A tacrolimus test system is a device intended to quantitatively determine tacrolimus concentrations as an aid in the management of transplant patients receiving therapy with this drug. This generic type of device includes immunoassays and chromatographic assays for tacrolimus.

(b) *Classification*. Class II (special controls). The special control is "Class II Special Controls Guidance Document: Cyclosporine and Tacrolimus Assays;

Guidance for Industry and FDA." See §862.1(d) for the availability of this guidance document.

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AWB
9/11/02

Linda S. Kahan

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

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