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DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Food and Drug Administration

21 CFR Part 866

[Docket No. 97P-0313]

Medical Devices; Reclassification and Codification of Fully Automated Short-Term Incubation Cycle Antimicrobial Susceptibility Devices From Class III to Class II

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is reclassifying the fully automated short-term incubation cycle antimicrobial susceptibility device for use in determining in vitro susceptibility of bacterial pathogens isolated from clinical specimens from class III to class II (special controls). The special control that will apply to this device is a guidance document entitled "Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA." The agency is also announcing that it has issued an order in the form of a letter to BioMerieux Vitek, Inc., reclassifying the device. The agency is classifying this device into class II because special controls, in addition to the general controls, will provide reasonable assurance of the safety and effectiveness of the device and there is sufficient information to establish special controls.

DATES: This rule is effective [insert date 90 days after date of publication in the Federal Register].

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FOR FURTHER INFORMATION CONTACT: Freddie M. Poole, Center for Devices and Radiological Health (HFZ-440), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 301-594-2096.

SUPPLEMENTARY INFORMATION:

I. Background (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 (the SMDA) (Public Law 101-629), and the Food and Drug Administration Modernization Act of 1997 (the FDAMA) (Public Law 105-115), 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, depending on 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 is insufficient information to show that general controls themselves will assure safety and effectiveness, but for which there is sufficient information to establish performance standards to provide such assurance. The SMDA broadened the definition of class II devices to mean devices for which there is insufficient information to show that general controls themselves will assure 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 guidance, recommendations, and any other appropriate actions the agency deems necessary (section 513(a)(1)(B) of the act).

Under section 513 of the act, devices that were in commercial distribution before May 28, 1976 (the date of enactment of the 1976 amendments), generally referred to as preamendments devices, are classified after FDA has: (1) Received a recommendation from a device classification panel (an FDA advisory committee); (2) published the panel's recommendation for comment, along with a proposed regulation classifying the device; and (3) published a final regulation classifying the device. FDA has classified most preamendments devices under these procedures.

Devices that were not in commercial distribution prior to 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: (1) The device is reclassified into class I or II; (2) FDA issues an order classifying the device into class I or II in accordance with new section 513(f)(2) of the act, as amended by the FDAMA; or (3) FDA issues an order finding the device to be substantially equivalent, under section 513(i) of the act, to a predicate device that does not require premarket approval. The agency determines whether new devices are substantially equivalent to previously offered 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 regulations (21 CFR part 807).

A preamendments device that has been classified into class III may be marketed, by means of 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.

Reclassification of postamendments devices is governed by section 513(f)(3) of the act, formerly section 513(f)(2) of the act. This section provides that FDA may initiate the reclassification of a device classified into class III under section 513(f)(1) of the act, or the manufacturer or importer of a device may petition the Secretary of Health and Human Services (the Secretary) for the issuance of an order classifying the device in class I or class II. FDA's regulations in § 860.134 (21 CFR 860.134) set forth the procedures for the filing and review of a petition for reclassification of such class III devices. In order to change the classification of the device, it is necessary that the proposed new class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use.

The FDAMA added a new section 513(f)(2) to the act which addresses classification of postamendments devices. New section 513(f)(2) of the act provides that, upon receipt of a "not substantially equivalent" determination, a 510(k) applicant may request FDA to classify a postamendments device into class I or class II. Within 60 days from the date of such a written request, FDA must classify the device by written order. If FDA classifies the device into class I or II, the applicant has then received clearance to market the device and it can be used as a predicate device for other 510(k)s. It is expected that this process will be used for low risk devices. This process does not apply to devices that have been classified by regulation into class III, i.e., preamendments class III devices, or class III devices for which a PMA is appropriate.

Under section 513(f)(3)(B)(i) of the act, formerly section 513(f)(2)(B)(i) of the act, the Secretary may, for good cause shown, refer a petition to a device classification panel. If a petition is referred to a panel, the panel shall make a recommendation to the Secretary respecting approval or denial of the petition. Any such recommendation shall contain: (1) A summary of the reasons for the recommendation, (2) a summary of the data upon which the recommendation is based, and (3) an identification of the risks to health (if any) presented by the device with respect to which the petition was filed.

II. Recommendation of the Panel

On July 2, 1997, FDA filed the reclassification petition submitted by BioMerieux Vitek, Inc., requesting reclassification of the fully automated short-term incubation cycle antimicrobial susceptibility devices from class III to class II. FDA consulted with the Microbiology Devices Panel (the panel). During an open public meeting on February 13, 1998, the panel unanimously recommended that FDA reclassify the fully automated short-term incubation cycle antimicrobial susceptibility device for use in determining in vitro susceptibility of bacterial pathogens isolated from clinical specimens from class III to class II. The panel identified the risks to health regarding use of this device as the reporting of erroneous results, citing that insufficient testing of each unique antimicrobial agent with an inappropriate clinical and challenge organism, the use of an uncalibrated inoculum, or a nonstandardized acceptable error endpoint can result in such erroneous reports.

FDA considered the panel's recommendations and tentatively agreed that the generic type of device, the fully automated short-term incubation cycle antimicrobial susceptibility device for use in determining in vitro susceptibility of bacterial pathogens isolated from clinical specimens, be

reclassified from class III to class II. Subsequently, in the **Federal Register** of March 8, 2000 (65 FR 12268), FDA issued a notice of the panel's recommendation for public comment.

After reviewing the information in the petition and presenting it before the panel, and after considering the panel's recommendation and the comments received in response to the notice of panel recommendation, FDA issued an order to the petitioner on December 28, 2001, reclassifying the fully automated short-term incubation cycle antimicrobial susceptibility device and substantially equivalent devices of this generic type, from class III to class II with the implementation of special controls. The special control applicable to this generic type of device is a guidance document entitled "Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA." FDA has identified the administration of an inappropriate antimicrobial agent to the patient as the risk to health associated with use of this device. The guidance document contains sections that discuss the use of appropriate challenge strains; standardized preparation of inoculum; the application of "acceptable error" as a range with confidence intervals; and appropriate clinical performance testing. In this way, the guidance will minimize the sources of erroneous reporting associated with the fully automated short-term incubation cycle antimicrobial susceptibility device. Testing and labeling recommendations are also discussed in the guidance document and also help manufacturers address the risk to health. Following the effective date of this final classification rule, any firm submitting a 510(k) premarket notification for a fully automated short-term incubation cycle antimicrobial susceptibility device 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.

Accordingly, as required by § 860.134(b)(6) and (b)(7) of the regulations, FDA is announcing the reclassification of the fully automated short-term incubation cycle antimicrobial susceptibility device from class III into class II. FDA is codifying the reclassification and the special control guidance by adding new § 866.1645. For the convenience of the reader, FDA is also adding a new § 866.1(e) to inform the reader where to find guidance documents referenced in 21 CFR part 866.

III. Environmental Impact

The agency has determined under 21 CFR 25.34(b) that this reclassification 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 notice 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 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 the device from class III to class II will relieve all manufacturers of the device of the cost of complying with the premarket approval requirements in section 515 of the act. Because reclassification will reduce regulatory costs with respect to this device, it will impose no significant economic impact on any small entities, and it may permit small potential competitors to enter the marketplace by lowering their costs. The agency therefore certifies that this rule will not have a significant economic impact on a substantial number of small entities. In addition, this rule will not impose costs of \$110 million or more on either the private sector or State, local, and tribal governments in the aggregate, and therefore a summary statement or analysis pursuant to 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 order and, consequently, a federalism summary impact statement is not required.

VI. Paperwork Reduction Act of 1995

This final rule contains no 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

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. Section 866.1 is amended by adding paragraph (e) to read as follows:

§ 866.1 Scope.

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

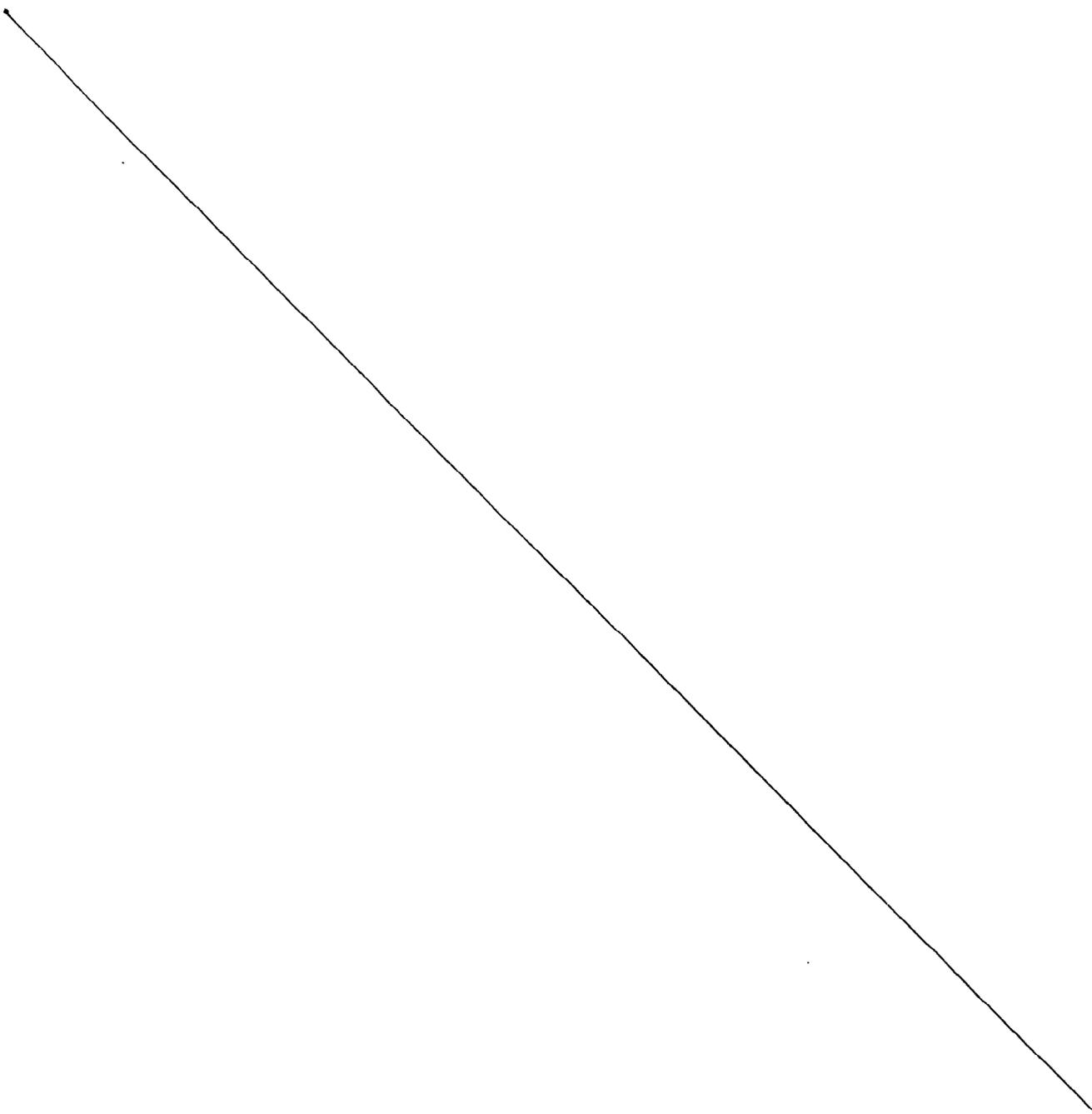
3. Section 866.1645 is added to subpart B to read as follows:

§ 866.1645 Fully automated short-term incubation cycle antimicrobial susceptibility system.

(a) *Identification.* A fully automated short-term incubation cycle antimicrobial susceptibility system is a device that incorporates concentrations of antimicrobial agents into a system for the purpose of determining in vitro susceptibility of bacterial pathogens isolated from clinical specimens. Test

results obtained from short-term (less than 16 hours) incubation are used to determine the antimicrobial agent of choice to treat bacterial diseases.

(b) *Classification.* Class II (special controls). The special control for this device is FDA's guidance document entitled "Class II Special Controls



Guidance Document: Antimicrobial Susceptibility Test (AST) Systems;
Guidance for Industry and FDA.”

Dated: 1/9/03
January 9, 2003.

Linda S. Kahan

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5 [FR Doc. ³02-~~00000~~ Filed ??-??-³02; 8:45 am]

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