(3) The sponsor's recommendation as to which agency component should have primary jurisdiction based on the mode of action that provides the most important therapeutic action of the combination product. If the sponsor cannot determine with reasonable certainty which mode of action provides the most important therapeutic action of the combination product, the sponsor's recommendation must be based on the assignment algorithm set forth in § 3.4(b) and an assessment of the assignment of other combination products the sponsor wishes FDA to consider during the assignment of its combination product.

* * * * *

Dated: August 9, 2005.

Jeffrey Shuren,

Assistant Commissioner for Policy.

[FR Doc. 05–16527 Filed 8–24–05; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 866

[Docket No. 2005N–0263]

Medical Devices; Immunology and Microbiology Devices; Classification of Ribonucleic Acid Preanalytical Systems

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is classifying ribonucleic acid (RNA) preanalytical systems into class II (special controls). The special control that will apply to the device is the guidance document entitled ''Class II Special Controls Guidance Document: RNA Preanalytical Systems (RNA Collection, Stabilization, and Purification Systems for RT–PCR Used in Molecular Diagnostic Testing).'' The agency is classifying the device into class II (special controls) in order to provide a reasonable assurance of safety and effectiveness of the device. Elsewhere in this issue of the **Federal Register**, FDA is announcing the availability of a guidance document that will serve as the special control for the device.

DATES: This rule is effective September 26, 2005. The classification was effective April 18, 2005.

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

SUPPLEMENTARY INFORMATION:

I. What is the Background of this Rulemaking?

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 (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, to a predicate device that does not require premarket approval.

The agency determines whether new devices are substantially equivalent to previous marketed devices by means of premarket notification procedures in section 510(k) of the act (21 U.S.C. 360(k)) and 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. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the **Federal Register** announcing such classification (section 513(f)(2) of the act).

In accordance with section 513(f)(1) of the act, FDA issued an order on February 18, 2005, classifying the PAXgene™ Blood RNA System into class III, because it 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 a device which was subsequently reclassified into class I or class II. On February 28, 2005, PreAnalytiX GmbH, c/o Becton, Dickinson and Co., submitted a petition requesting classification of the PAXgene™ Blood RNA System under section 513(f)(2) of the act. The manufacturer recommended that the device be classified into class II.

In accordance with 513(f)(2) of the act, FDA reviewed the petition in order to classify the device under the criteria for classification set forth in 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 PAXgene™ Blood RNA System can be classified into class II with the establishment of special controls. FDA believes these special controls will provide reasonable assurance of the safety and effectiveness of the device.

The device is assigned the generic name RNA Preanalytical Systems and it is identified as a device intended to collect, store, and transport patient specimens, and stabilize intracellular RNA from the specimens, for subsequent isolation and purification of the intracellular RNA for reverse transcriptase polymerase chain reaction (RT–PCR) used in in vitro molecular diagnostic testing. The device may consist of sample collection devices, nucleic acid isolation and purification reagents, and processing reagents/equipment (tubes, columns, etc.). It also may contain instruments for automation of the nucleic acid isolation and purification steps.

FDA has identified the following risks to health associated specifically with this type of device: (1) Inaccurate results and improper patient management, (2) delay in diagnosis, and (3) a need for patient specimen recollection.

Failure of the system during specimen collection, or during RNA stabilization or purification could yield an RNA sample of low quality and quantity. Low quality RNA, when tested, could result in falsely low or falsely high RNA transcript signal levels leading to inaccurate diagnosis and/or improper patient management. Low quantity of RNA could render the samples unusable for downstream RT–PCR applications; specimens would need to be recollected, causing possible delay in diagnosis. In addition, depending on specimen type, recollection could pose additional patient risk (e.g., tissue biopsy). The degree of risk varies depending on the disease or condition/stage being diagnosed or managed. Results of RNA testing should always be considered in conjunction with other clinical factors.

FDA believes that the class II special controls guidance document aids in mitigating the potential risks to health by providing recommendations on validation of performance characteristics, including RNA stability, purity, integrity, yield, repeatability, reproducibility, and suitability for use in RT–PCR assays. The guidance document also provides information on how to meet premarket (510(k)) submission requirements for the device. FDA believes that the special controls guidance document, in addition to general controls, addresses the risks to health identified previously and provides reasonable assurance of the safety and effectiveness of the device. Therefore, on April 18, 2005, FDA issued an order to the petitioner classifying the device into class II. FDA is codifying this device by adding § 866.4070.

Following the effective date of this final classification rule, any firm submitting a 510(k) premarket notification for an RNA preanalytical system will need to address the issues covered in the special controls guidance. However, the firm 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 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. For this type of device, FDA has determined that premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device and, therefore, the 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, prior to marketing the device, which contains information about the RNA Preanalytical Systems they intend to market.

II. What is the Environmental Impact of This Rule?

The agency has determined under 21 CFR 25.34(b) that this action is of 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.

III. What is the Economic Impact of This Rule?

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 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 $115 million, using the most current (2003) 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.

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. How Does This Rule Comply With the 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.

VI. What References Are on Display?

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 PreAnalytiX GmbH, c/o Becton, Dickinson and Co., dated February 28, 2005.

List of Subjects in 21 CFR Part 866

Medical devices.

n 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

n 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.

n 2. Section 866.4070 is added to subpart E to read as follows:

§866.4070 RNA Preanalytical Systems.

(a) *Identification*. RNA Preanalytical Systems are devices intended to collect, store, and transport patient specimens, and stabilize intracellular RNA from the specimens, for subsequent isolation and purification of the intracellular RNA for RT–PCR used in in vitro molecular diagnostic testing.

(b) *Classification*. Class II (special controls). The special control is FDA's guidance document entitled ''Class II Special Controls Guidance Document: RNA Preanalytical Systems (RNA Collection, Stabilization and Purification System for RT–PCR Used in Molecular Diagnostic Testing).'' See § 866.1(e) for the availability of this guidance document.

Dated: August 9, 2005.

Linda S. Kahan,

Deputy Director, Center for Devices and Radiological Health.

[FR Doc. 05–16914 Filed 8–24–05; 8:45 am]

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DEPARTMENT OF THE TREASURY

Internal Revenue Service

26 CFR Part 1

[TD 9222]

RIN 1545–BD49

Guidance Under Section 951 for Determining Pro Rata Share

AGENCY: Internal Revenue Service (IRS), Treasury.

ACTION: Final regulations.

SUMMARY: This document contains final regulations under section 951(a) of the Internal Revenue Code (Code) that provide guidance for determining a United States shareholder's pro rata share of a controlled foreign corporation's (CFC's) subpart F income, previously excluded subpart F income withdrawn from investment in less developed countries, and previously excluded subpart F income withdrawn from foreign base company shipping operations.

DATES: *Effective Date:* These regulations are effective August 25, 2005.

Applicability Date: For dates of applicability, see § 1.951–1(e)(7).

FOR FURTHER INFORMATION CONTACT: Jeffrey L. Vinnik, (202) 622–3840 (not a toll-free number).

SUPPLEMENTARY INFORMATION:

Background

On August 6, 2004, the IRS published in the **Federal Register** a notice of proposed rulemaking (REG–129771–04, 2004–36 I.R.B. 453) under section 951 of the Code. Written comments were received in response to the notice of proposed rulemaking. No public hearing was requested or held on the notice of proposed rulemaking. After consideration of the comments received, the proposed regulations are adopted as final regulations with the modifications discussed below. This issue of the **Federal Register** also includes a notice of proposed rulemaking (REG–129782–05) setting forth special pro rata share rules that apply to (1) a CFC with more than one class of stock which has earnings and profits and subpart F income for the taxable year that are attributable to one or more deemed dividends arising from one or more transactions described in section 304 that are part of a plan a principal purpose of which is the avoidance of Federal income taxation, and (2) a CFC with certain cumulative preferred stock outstanding that is held by one or more persons who are not U.S. taxpayers.

Summary of Public Comments and Explanation of Changes

A. Amounts Determined Under Section 956 of the Code

Section 951(a)(1) requires a United States shareholder of a CFC to include in income the amount determined under section 956 with respect to such shareholder. The proposed regulations include a conforming change to replace *increase in earnings invested in United States property* with *amount determined under section 956* to reflect statutory changes made to section 956 of the Code by the Omnibus Budget Reconciliation Act of 1993, Public Law 103–66 (107 Stat. 312). Commentators recommended that the pro rata rules for section 956 be addressed in a separate regulatory project because, after the statutory change to section 956, the section 951 pro rata rules are no longer relevant to a United States shareholder's inclusion of the amount determined under section 956.

The IRS and Treasury Department agree with this recommendation and accordingly have deleted all references to section 956 under § 1.951–(1)(e). Provisions of § 1.951–1(a) and (d) that concerned a United States shareholder's pro rata share of the CFC's increase in earnings invested in United States property have been revised and removed, respectively, to conform the regulations to the relevant post-1993 Code provisions. The IRS and Treasury Department are considering a separate regulations project regarding the amount determined under section 956.

B. One Class of Stock—Proposed § 1.951–1(e)(2)

The proposed regulations state that if a CFC for a taxable year has only one class of stock outstanding, each United States shareholder's pro rata share of such corporation's subpart F income for the taxable year is determined by allocating the CFC's earnings and profits for such year on a per-share basis. A commentator asked that this rule be modified to clarify that the relevant earnings and profits are earnings and profits for such year unreduced by distributions during the year.

The IRS and Treasury Department agree with the comment and have clarified § 1.951–1(e)(2) accordingly.

C. More Than One Class of Stock—Proposed § 1.951–1(e)(3)(i)

In general, the proposed regulations allocate subpart F income among multiple classes of stock by reference to the distributions that would be made with respect to each class if the CFC's earnings and profits for the year were distributed on the last day of the CFC's taxable year (the hypothetical distribution). A commentator expressed concern that the hypothetical-distribution rule under the proposed regulations could allocate earnings and profits to preferred stock (including, *e.g.*, preferred stock with a noncumulative dividend preference) without regard to whether or when dividends are or will be paid. The commentator recommended that the proposed regulations be amended to provide that dividend rights should not be taken into account if, as of an appropriate date, the dividends have not been paid.

The IRS and Treasury Department have considered this comment and have concluded that, if the terms of a class of preferred stock are such that an obligation to pay a dividend with respect to the stock may or may not arise during the CFC's taxable year, depending on an exercise of discretion by the CFC's board of directors or a similar governing body, then the stock should be considered to have discretionary distribution rights. In such case, the rule of § 1.951–1(e)(3)(ii) would apply. Therefore, the suggested amendment was not adopted.

A commentator recommended that, in the case of mandatorily redeemable preferred stock with cumulative dividend rights, the regulation should include an anti-abuse rule to be applied where the amount of earnings and profits required to be allocated to such stock differs substantially on a present-value basis from the amount expected to be distributed on such stock. Additionally, a commentator recommended that an anti-abuse rule could target shareholder-level agreements that are inconsistent with the economic terms of the underlying stock.

The IRS and Treasury Department agree that it is appropriate to provide a special rule for the allocation of earnings and profits to certain mandatorily redeemable cumulative preferred stock held by persons who are not U.S. taxpayers. This special rule is set forth in a notice of proposed rulemaking published in this issue of the **Federal Register** (REG–129782–05).

With respect to the comments regarding shareholder-level agreements,