

## **DEPARTMENT OF HEALTH AND HUMAN SERVICES**

### **Food and Drug Administration**

#### **21 CFR Part 1271**

**[Docket No. 97N-484R]**

### **Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing**

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

**ACTION:** Interim final rule; opportunity for public comment.

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**SUMMARY:** The Food and Drug Administration (FDA) is issuing an interim final rule to except human dura mater and human heart valve allografts, currently subject to application or notification requirements under the Federal Food, Drug, and Cosmetic Act (the act), from the scope of the definition of “human cells, tissues, or cellular or tissue-based products (HCT/P’s)” subject to the registration and listing requirements contained in 21 CFR part 1271. That definition became effective on January 21, 2004. FDA is taking this action to assure that these products, which are currently subject to the act and therefore regulated under the current good manufacturing practice regulations set out in the quality system regulations in 21 CFR part 820 are not released from the scope of those regulations before a more comprehensive regulatory framework applicable to HCT/P’s, including donor suitability requirements, good tissue practice regulations, and appropriate enforcement provisions, is fully in place. When that comprehensive framework is in place, FDA intends that human dura mater and human heart valves will be subject to it. FDA intends to revoke this interim final rule at that time.

**DATES:** The interim final rule is effective January 23, 2004. The compliance date is [*insert date 60 days after date of publication in the Federal Register*]. Submit written or electronic comments on the interim final rule by [*insert date 90 days after date of publication in the Federal Register*].

**ADDRESSES:** Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://www.fda.gov/dockets/ecomments>.

**FOR FURTHER INFORMATION CONTACT:** Paula S. McKeever, Center for Biologics Evaluation and Research (HFM-17), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1448, 301-827-6210.

**SUPPLEMENTARY INFORMATION:**

**I. Background**

In an earlier related rulemaking entitled “Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing” (66 FR 5447, January 19, 2001), the agency defined an HCT/P as “articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient.” Examples of HCT/P’s included, but were not limited to, ligaments, skin, bone, dura mater, heart valves, corneas, peripheral and cord blood hematopoietic stem cells, manipulated autologous chondrocytes, oocytes, and spermatozoa (66 FR at 5447 at 5467).

That rule further provided that HCT/P’s meeting the criteria established in part 1271 (21 CFR part 1271) in § 1271.10 would be regulated solely under section 361 of the Public Health Service Act (the PHS Act) (42 U.S.C. 264). The effect of these two provisions was that human dura mater and human heart

valve allografts meeting the definition of HCT/P and the criteria in § 1271.10 for regulation solely under section 361 of the PHS Act would be removed from the scope of regulations established under the authority of the act. Instead they would be regulated solely under the comprehensive HCT/P regulations that the agency intended to issue under the authority of section 361 of the PHS Act. The agency intended to replace the current good manufacturing practice requirements applicable to human dura mater and human heart valve allografts, which provide protection against the risks of communicable disease and are set out in the Quality System Regulation under part 820 (21 CFR part 820), with donor suitability and good tissue practice regulations, which would be developed specifically to address the risks of communicable disease transmission.

Accordingly, at the time the registration and listing rule published, FDA had proposed two other rules to establish the remainder of that comprehensive regulatory framework:

- Suitability Determination for Donors of Human Cellular and Tissue-Based Products (64 FR 52696, September 30, 1999), and
- Current Good Tissue Practice for Manufacturers of Human Cellular and Tissue-Based Products; Inspection and Enforcement (66 FR 1508, January 8, 2001).

When finalized, these three rules will establish a comprehensive regulatory framework for human cellular and tissue-based products, to be contained in part 1271. However, because all three regulations were not in place at the time the registration and listing rule published, the agency delayed, initially for 2 years, the effective date of the definition of HCT/P previously quoted. The agency made the registration and listing rule effective

at first only for products currently regulated as human tissue intended for transplantation under 21 CFR part 1270. The agency explained that FDA did not intend to begin regulating human dura mater and human heart valve allografts that meet the criteria for regulation solely under section 361 of the PHS Act until the donor-suitability and good tissue practice (GTP) components of part 1271 become effective, or other appropriate steps have been taken. (66 FR at 5447 at 5453). Because finalizing the remaining two rules presented difficult issues and the rulemaking has taken more time than initially foreseen, FDA delayed the effective date for an additional year, until January 21, 2004 (68 FR 2689, January 21, 2003).

We (FDA) have now reached that date, and although work on the remaining two rules is nearing completion, the rules have not yet published. Rather than again delay the effective date of this provision, FDA believes that the provision should take effect, provided that the agency issues this interim final rule to assure that human dura mater and human heart valve allografts remain subject to appropriate provisions under the act, and including current good manufacturing practice requirements, until the comprehensive regulatory framework is in place. (FDA understands that many establishments may have reasonably expected FDA to delay the effective date of this provision again, because the donor suitability and GTP rules are not yet finalized. Once the comprehensive framework is in place, the agency intends to revoke this interim final rule, so that the comprehensive regulatory framework would then apply to human dura mater and human heart valve allografts, and these products would no longer be subject to regulation as medical devices under the act.

## **II. Legal Authority**

FDA is issuing this regulation under the authority of section 361 of the PHS Act. Under that section, FDA may make and enforce regulations necessary to prevent the introduction, transmission, or spread of communicable diseases between the States or from foreign countries into the States. (See sec. 1, Reorg. Plan No. 3 of 1966 at 42 U.S.C. 202 for delegation of section 361 of the PHS Act authority from the Surgeon General to the Secretary of the Department of Health and Human Services (the Secretary); See 21 CFR 5.10(a)(4) for delegation from the Secretary to FDA.) Intrastate transactions affecting interstate communicable disease transmission may also be regulated under section 361 of the PHS Act. (See *Louisiana v. Mathews*, 427 F. Supp. 174, 176 (E.D. La. 1977).) Until we put into place the new regulatory framework's remaining components, which are intended to prevent the introduction, transmission, and spread of communicable diseases, it is necessary to preserve the applicability of regulations currently applicable to human dura mater and human heart valve allografts.

## **III. Issuance of an Interim Final Rule; Immediate Effective Date**

Under the provisions of the Administrative Procedure Act at 5 U.S.C. 553(b)(B) and FDA's administrative practices and procedures regulations at § 10.40(e)(1) (21 CFR 10.40(e)(1)), the Commissioner of Food and Drugs (the Commissioner) finds that use of prior notice and comment procedures for issuing this interim final rule is contrary to the public interest. In addition, the Commissioner finds good cause under 5 U.S.C. 553(d)(3) and § 10.40(c)(4)(ii) for making this interim final rule effective immediately upon filing at the Office of the Federal Register.

FDA concludes that this interim final rule is necessary to assure that human dura mater and human heart valve allografts, currently subject to good manufacturing practice regulatory requirements under the authority of the act, do not lose that protection during an interim period occurring between the date of their incorporation into the definition of HCT/P (January 21, 2004) and the effective date for the tissue donor suitability and GTP rules, to be finalized in the near future. Human dura mater and human heart valve allografts present significant risks of communicable disease transmission when the products are not handled properly. Absent this interim final rule, human dura mater and human heart valve allografts would fall within the definition of HCT/P's (§ 1271.3(d)(2)), and likely would also fall within the criteria for regulation solely under section 361 of the PHS Act (§ 1271.10). This would mean that human dura mater and human heart valve allografts would no longer be subject to the quality system regulation currently applicable to devices (part 820). If this occurred before the donor suitability and GTP rules became final, the public would lose the important public health protections afforded by the quality system regulation. In light of the significant public health risk that would be presented by these products if their manufacture were not subject to either a good tissue practice or current good manufacturing practice regulation, the Commissioner finds good cause to make these regulatory requirements final and effective immediately.

Although this agency is publishing this regulation as an interim final rule without an opportunity for prior notice and comment on a proposed rule, FDA is providing opportunity for comment on this interim final rule.

#### **IV. Provisions of the Interim Final Rule**

This interim final rule amends § 1271.3(d)(2) to delete the words “dura mater and heart valves” from the definition of “Human cells, tissues, or cellular or tissue-based products (HCT/P’s).” It further adds new § 1271.3(d)(2)(viii), an exception to the definition of HCT/P’s for human dura mater and human heart valve allografts. A minor change was necessary to § 1271.3(d)(2)(vi) and (d)(2)(vii) due to the addition of § 1271.3(d)(2)(viii).

#### **V. Analysis of Impacts**

FDA has examined the impacts of the interim final rule under Executive Order 12866 and the Regulatory Flexibility Act (Public Law 104–4), and the Unfunded Mandates Reform Act of 1995 (2 U.S.C. 1531–1571), which are not applicable to interim final rules. 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 interim final rule is consistent with the regulatory philosophy and principles identified in the Executive order. In addition, the interim final rule is not a significant regulatory action as defined by the Executive order. Therefore, FDA is not required under the Executive order to submit it to Office of Management and Budget (OMB) for review.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of proposed and final rules on small entities. Because this rule actually narrows the scope of the current regulation, this interim final rule does not impose in any new requirements. The agency certifies that the interim final rule will not have a significant

economic impact on a substantial number of small entities. The Regulatory Flexibility Act requires no further analysis of this interim final rule.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement of anticipated costs and benefits, before issuing any final rule that was the subject of a notice of proposed rulemaking and that may result in the expenditure in any 1 year by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100 million or more (adjusted annually for inflation). The current inflation adjusted statutory threshold is about \$110 million. FDA does not expect this interim final rule to result in any 1-year expenditure that would meet or exceed this amount. FDA is not required to prepare a written statement under the Unfunded Mandates Reform Act of 1995.

#### **VI. The Paperwork Reduction Act of 1995**

This interim final rule contains no collections of information. Therefore, clearance by OMB under Paperwork Reduction Act of 1995 is not required.

#### **VII. Environmental Impact**

The agency has determined under 21 CFR 25.30(i) and 21 CFR 25.30(j) 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.

#### **VIII. Federalism**

FDA has analyzed this interim final rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the interim final 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 interim final 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.

## **IX. Request for Comments**

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this interim final rule. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

## **List of Subjects**

### *21 CFR Part 1271*

Biologics, Drugs, Human cells and tissue-based products, Medical devices, Reporting and recordkeeping requirements.

■ Therefore, under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 1271 is amended as follows:

### **PART 1271—HUMAN CELLS, TISSUES, AND CELLULAR AND TISSUE– BASED PRODUCTS**

■ 1. The authority citation for 21 CFR part 1271 continues to read as follows:

**Authority:** 42 U.S.C. 216, 243, 264, 271.

■ 2. Section 1271.3 is amended by revising the second sentence in the introductory text of paragraph (d)(2), by revising paragraphs (d)(2)(vi) and (d)(2)(vii), and by adding paragraph (d)(2)(viii) to read as follows:

**§ 1271.3 How does FDA define important terms in this part?**

\* \* \* \* \*

(d) \* \* \*

(2) \* \* \* Examples of HCT/P's include, but are not limited to, bone, ligament, skin, cornea, hematopoietic stem cells derived from peripheral and cord blood, manipulated autologous chondrocytes, epithelial cells on a synthetic matrix, and semen or other reproductive tissue.\* \* \*

\* \* \* \* \*

(vi) Cells, tissues, and organs derived from animals other than humans;

(vii) In vitro diagnostic products as defined in § 809.3(a) of this chapter;

and

(viii) Human dura mater and human heart valve allografts.

\* \* \* \* \*

Dated: January 21, 2004.

**Jeffrey Shuren,**

*Assistant Commissioner for Policy.*

[FR Doc. 04-????? Filed ??-??-04; 8:45 am]

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