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DEPARTMENT OF HEALTH AND HUMAN SERVICES

42 CFR Part 121

RIN 0906-AB02

Change to the Definition of “Human Organ” under Section 301 of the National Organ Transplant Act of 1984

AGENCY: Health Resources and Services Administration, HHS.

ACTION: Notice of proposed rulemaking.

SUMMARY: This notice seeks public comment on the proposed change in the definition of “human organ” in section 301 of the National Organ and Transplant Act of 1984, as amended, (NOTA) to explicitly incorporate hematopoietic stem cells (HSCs) within peripheral blood in the definition of “bone marrow.” This would clarify that the prohibition on transfers of human organs for valuable consideration applies to HSCs regardless of whether they were recovered directly from bone marrow (by aspiration) or from peripheral blood (by apheresis). This amendment will also conform section 301 to the provisions of the Stem Cell Research and Therapeutic Act of 2005, as amended.

DATES: To be considered, comments should be submitted by [INSERT 60 DAYS FROM DATE OF PUBLICATION IN THE FEDERAL REGISTER]. Subject to consideration of the comments submitted, the Department intends to publish final regulations.

ADDRESSES: You may submit comments, identified by Regulatory Information Number RIN 0906-AB02, by any of the following methods, but the first option is preferred:

- *Federal eRulemaking Portal:* <http://www.regulations.gov>. Follow the instructions for submitting comments.

- *Agency Website:* <http://www.hrsa.gov/>. Follow the instructions for submitting comments on the Agency Website.
- *Email:* SGrant@hrsa.gov. Include RIN 0906-AB02 in the subject line of the message.
- *Fax:* (301) 594-6095.
- *Mail:* Shelley Grant, MHSA, Branch Chief, Blood Stem Cell Transplantation Program, Division of Transplantation, Healthcare Systems Bureau, Health Resources and Services Administration, 5600 Fishers Lane, Room 12C-06, Rockville, Maryland 20857.

Instructions: All submissions must include the agency name and RIN for this rulemaking. All comments received will be posted without change to <http://www.hrsa.gov/>, including any personal information provided. Additional information concerning the submission of comments and/or the rulemaking process can be obtained from the Regulations Officer, Division of Policy Information and Coordination, Health Resources and Services Administration, 5600 Fishers Lane, Room 14-101, Rockville, Maryland 20857.

Docket: For access to the docket to read background documents or comments received, go to the Division of Transplantation, Healthcare Systems Bureau, Health Resources and Services Administration, 5600 Fishers Lane, Room 12C-06, Rockville, Maryland 20857, weekdays (Federal holidays excepted) between the hours of 8:30 a.m. and 5 p.m. To schedule an appointment to view public comments, phone (301) 443-7757.

FOR FURTHER INFORMATION CONTACT: Shelley Grant, MHSA, at the above address; telephone number (301) 443-8036.

SUPPLEMENTARY INFORMATION:

I. Background

A. Statutory Background

Congress enacted the National Organ Transplant Act of 1984 (NOTA), Pub. L. 98-507, to develop a national comprehensive policy regarding organ transplantation. Within NOTA, section 301 criminalizes the transfer of organs for use in human transplantation for “valuable consideration.” “Human organ” is defined to include “bone marrow . . . or any subpart thereof” or any organ specified by the Secretary in regulation. NOTA section 301(c)(1) [codified at 42 U.S.C. 274e(c)(1)]. The law criminalizes the transfer of any human organ for valuable consideration with a fine of up to \$50,000 and imprisonment up to five years. Though the general prohibition has been in place since 1984, Congress has made numerous amendments to NOTA and otherwise has focused recurring attention on organ and bone marrow donation and transplantation. In 1988, Congress specifically amended section 301 to broaden the definition of “human organ” to include “any subpart thereof.” Organ Transplant Amendments of 1988, Pub. L. 100-607, section 407, 102 Stat. 3048, 3116 (Nov 4, 1988). Congress again amended section 301 in 2007 to exclude paired donation from the definition of “valuable consideration.” Charlie Norwood Living Organ Donation Act. Sec. 102, Pub. L. 110-144, section 102, 121 Stat. 1813 (2007).

When enacted, NOTA provided for a demonstration study on the feasibility of a “national registry of voluntary bone marrow donors.” Sec. 401, Pub. L. 98-507, 98 Stat. 2347 (1984). In 1988, in the same law which broadened the definition of organ to “any subpart thereof,” Congress directed the Secretary to establish a national bone marrow registry. Sec. 404, Pub. L. 100-607, 102 Stat. 3116 (1988). Subsequently, Congress established the National Bone Marrow Donor Registry. Transplant Amendments Act of 1990. Sec.101, Pub. L. 101-616, 104 Stat. 3279 (1990). The National Bone Marrow Donor Registry is now called the C.W. Bill Young Cell Transplantation Program, Pub. L. 109-129, 119 Stat. 2250 (2005) [42 U.S.C. 274k, *et seq.*].

Enacted in 2005, and reauthorized in 2010, the statute defines “bone marrow” as “the cells found in adult bone marrow *and* peripheral blood.” 42 U.S.C. 274l-1 (emphasis added).

B. Scientific Development

Hematopoietic stem cells (HSCs) originate in the spongy tissue within bones commonly referred to as “bone marrow” and give rise to mature blood cells, namely red blood cells, white blood cells, and platelets. HSCs are found in the highest concentration in bone marrow and in lower concentrations in circulating (peripheral) blood. What are commonly referred to as “bone marrow” transplants are actually transplants of hematopoietic stem cells, regardless of source. “Bone marrow” transplantation (*i.e.*, HSC transplantation) is commonly used to treat certain blood cancers like leukemia, other blood diseases like aplastic anemia, and immune-deficiency diseases.

Until recently, available techniques required that HSCs be obtained from the marrow by inserting a needle into the marrow to extract liquid containing the HSCs. The extracted material is then put through a filtration process to separate HSCs from other marrow components and concentrate them, before the HSCs are then transplanted into the transplant recipient. This type of HSC collection is known as the “aspiration method.”

Under a newer process, known as peripheral blood stem cell apheresis, donors receive five daily injections of an HSC stimulating drug that causes increased production and mobilization of HSCs from the bone marrow into the circulating blood stream (peripheral blood). Once these drug doses have been administered, a sufficient quantity and concentration of HSCs become available for retrieval in a donor’s peripheral blood. At this point, a needle is inserted into one of the donor’s peripheral or central veins, and his or her blood then passes through an apheresis machine that isolates and collects the hematopoietic stem cells. The remaining blood

components are then returned to the donor through the intravenous catheter. The apheresis collection procedure can take up to eight hours. Most apheresis donations occur in one daylong session, although some are completed over the course of two days. A donor's total blood volume is run through the process three to five times to collect a sufficient number of hematopoietic stem cells necessary for successful transplantation. The C.W. Bill Young Cell Transplantation Program and its predecessor program, the National Bone Marrow Donor Registry, have coordinated apheresis donations since 1999. U.S. General Accounting Office, *Bone Marrow Transplants: Despite Recruitment Success, National Program may be Underutilized* 6 (2002). Hematopoietic stem cells themselves have always been recognized as the critical component of bone marrow donation. *Thomas' Hematopoietic Cell Transplantation* 36-37, 72-7, 618 (Frederick Appelbaum, *et al.*, eds. 4th ed. 2009).

Though safer and less invasive than aspiration, apheresis still carries risks to the donor. Side-effects of the HSC stimulating drug may include rupture of the spleen or a low platelet count (thrombocytopenia). There may also be serious risks related to the placement of a central venous line in larger veins (jugular, subclavian, or femoral) in donors without adequate peripheral vein access. More importantly, aspiration is the medically indicated method of donation for a substantial number of transplants. *American Society of Hematology*, "Increased Incidence of Chronic Graft-Versus-Host Disease (GVHD) and No Survival Advantage with Filgrastim-Mobilized Peripheral Blood Stem Cells (PBSC) Compared to Bone Marrow (BM) Transplants From Unrelated Donors: Results of Blood and Marrow Transplant Clinical Trials Network (BMT CTN) Protocol 0201, a Phase III, Prospective, Randomized Trial," Anasetti, Claudio, Confer, Dennis, *et al.*, 2011; *Biology of Blood and Marrow Transplantation*, "Peripheral Blood Grafts from Unrelated Donors Are Associated with Increased Acute and

Chronic Graft-Versus-Host Disease without Improved Survival,” Eapen, Mary, Anasetti, Claudio, *et al.*, 2007. It is important to note that, even assuming the relative safety of apheresis, a substantial number of potential transplant recipients will continue to require HSCs obtained by aspiration.

Congress has consistently updated the law as advances in organ donation technology have been made. As noted above, Congress expanded the scope of NOTA’s definition of organ in 1988 to include “any subpart thereof.” In the 2005 Act, Congress defined “bone marrow” to include HSCs in the “peripheral blood.” And, as previously stated, Congress expressly granted the Secretary authority to define organs through regulation as the field of transplantation evolves.

C. Litigation

On March 27, 2012, a panel of the United States Ninth Circuit Court of Appeals issued an opinion holding that bone marrow donors may be compensated if the apheresis method of donation is used. *Flynn v. Holder*, 684 F.3d 852 (9 Cir. 2012). The plaintiffs in the case alleged that the ban on sale of “bone marrow” under NOTA lacked a “rational basis” under the equal protection clause of the Fifth Amendment. Plaintiffs sought to operate a program offering \$3,000 awards, in the form of scholarships, housing allowances, or gifts to charity, to bone marrow donors. The district court found multiple rational bases for the prohibition. However, the Ninth Circuit panel held there was no constitutional question since the apheresis method of marrow harvesting was not covered by the statutory prohibition on the transfer of organs for “valuable consideration.”

In rejecting the government’s arguments that bone marrow included HSCs in the peripheral blood, the Ninth Circuit panel instead focused on the recent development of apheresis technology as foreclosing the possibility that Congress intended the NOTA, when enacted, to

cover HSCs in the blood stream. Since apheresis was not used to procure HSCs in 1984, the Court held that Congress could not have intended HSCs obtained through this method to fall under the ban in section 301. Therefore, the Ninth Circuit panel believed that the non-commodification principle and other negative consequences Congress sought to avoid were not relevant to HSCs in the peripheral blood. Importantly, however, the Ninth Circuit panel did recognize in its written opinion that the Secretary had regulatory authority to define peripheral blood stem cells as organs. The effect of exercising this authority through this proposed amendment is to clarify that HSCs are covered by the prohibition on transfers of human organs for valuable consideration found in NOTA section 301(c)(1) [codified at 42 U.S.C. 274e(c)(1)].

While focused on the proposal of the plaintiffs before it, the Court's holding does not limit the compensation donors can demand to scholarships, housing allowances, or charitable gifts. Particularly in light of the much more stringent matching required between donor and recipient for HSC transplants to be successful, the opportunities for exploitation of those in medical need of HSC transplantation are much greater than for solid organ transplantation.

II. Proposed Rule

In light of the Congressional, Departmental, and scientific community's long understanding of bone marrow as encompassing HSCs in peripheral blood, the Department is proposing to amend the definition of "human organ" in section 301 to explicitly include HSCs in peripheral blood as part of the definition of "bone marrow" for the purposes for section 301. Notwithstanding the Ninth Circuit's decision in the *Flynn* case, the statute expresses a Congressional intent to ban the commodification of HSCs that are used in human transplants, curb opportunities for coercion and exploitation, encourage altruistic donations, and decrease the likelihood of disease transmission resulting from paid donations. Furthermore, the Department

has clear regulatory authority to clarify the regulatory definition of “human organ” to make explicit that the prohibition applies to both types of collection methods (apheresis and aspiration) – authority that the Ninth Circuit expressly recognized.

For these reasons, the Department is proposing to amend 42 CFR 121.13 to read: “Human organ” as covered by section 301 of the National Organ Transplant Act, as amended, means the human (including fetal) kidney, liver, heart, lung, pancreas, bone marrow and other hematopoietic stem/progenitor cells without regard to the method of their collection, cornea, eye, bone, skin, and intestine, including the esophagus, stomach, small and/or large intestine, or any portion of the gastrointestinal tract.” The Department has amended, and proposed to amend, the definition of “human organ” on several occasions, as medical knowledge has progressed. *See* 72 FR 10616 (March 9, 2007) (defining prohibition in section 301 to include intestines), and 76 FR 78216 (December 16, 2011) (proposing to include vascularized composite allografts in the definition of “human organ”). The proposed change will clarify that the meaning of “bone-marrow,” for purpose of the prohibition, does not hinge on the collection method used to obtain the cells. The proposed change to the definition of “human organ” in section 301 does not affect the Food and Drug Administration’s regulation of whole blood and blood components, and of human cells, tissues, and cellular-and tissue-based products (HCT/Ps).

III. Impact Analysis

Executive Order 12866 and Paperwork Reduction Act

Economic and Regulatory Impact

Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when rulemaking is necessary, to select regulatory approaches that provide the greatest net benefits (including potential economic, environmental, public health,

safety, distributive, and equity effects). In addition, under the Regulatory Flexibility Act, if a rule has a significant economic effect on a substantial number of small entities the Secretary must specifically consider the economic effect of a rule on small entities and analyze regulatory options that could lessen the impact of the rule.

The Secretary has determined that minimal resources are required to implement the requirements in this rule because the organizations involved (*e.g.*, marrow registries and transplant hospitals) currently implement their programs in accordance with the procedures announced in this proposed rule. Therefore, in accordance with the Regulatory Flexibility Act of 1980 (RFA), and the Small Business Regulatory Enforcement Act of 1996, which amended the RFA, the Secretary certifies that this rule will not have a significant impact on a substantial number of small entities.

The Secretary also has determined that this proposed rule does not meet the criteria for a major rule as defined by Executive Order 12866 and would not have a major effect on the economy or Federal expenditures. We have determined that the proposed rule is not a major rule within the meaning of the statute providing for Congressional Review of Agency Rulemaking, 5 U.S.C. 801. Similarly, it will not have effects on state, local, and tribal governments or on the private sector such as to require consultation under the Unfunded Mandates Reform Act of 1995.

The provisions of this rule will not affect the following elements of family well-being: family safety, family stability, marital commitment; parental rights in the education, nurture, and supervision of their children; family functioning, disposable income, or poverty; or the behavior and personal responsibility of youth, as determined under section 654(c) of the Treasury and General Government Appropriations Act of 1999.

Section 202 (a) of the Unfunded Mandates Reform Act of 1995 requires that agencies assess anticipated costs and benefits before issuing any rule that includes a federal mandate that could result in expenditure in any one year by state, local, or tribal governments, in the aggregate, or by the private sector, of \$100 million in 1995 dollars, updated annually for inflation. The current threshold after adjustment for inflation using the Implicit Price Deflator for Gross Domestic Product is about \$141 million. This rule would not meet or exceed that threshold.

This rule is not economically significant under section 3(f) of Executive Order 12866 and is not being treated as a “significant regulatory action” under section 3(f). Accordingly, the rule has not been reviewed by the Office of Management and Budget.

As stated above, this proposed rule would modify the regulations governing the nation’s Organ Procurement and Transplantation Network (OPTN) and section 301 of NOTA based on legal authority.

Paperwork Reduction Act of 1995

The amendments proposed in this Rule will not impose any additional data collection requirements beyond those already imposed under the current information collection requirements, which have been approved by the Office of Management and Budget (OMB No. 0915-0310). The currently approved data collection includes worksheets and burden for all marrow transplants.

List of Subjects in 42 CFR Part 121

Healthcare, Hospitals, Organ transplantation.

Dated: September 19, 2013.

Mary K. Wakefield,

Administrator,

Health Resources and Services Administration

Approved: September 25, 2013.

Kathleen Sebelius,

Secretary.

Therefore, under the authority of section 301 of NOTA, as amended, and for the reasons stated in the preamble, the Department proposes to amend 42 CFR part 121 as follows:

PART 121—ORGAN PROCUREMENT AND TRANSPLANTATION NETWORK

1. The authority citation continues to read as follows:

Sections 215, 371-376 of the Public Health Service Act (42 U.S.C. 216, 273-274d); sections 1102, 1106, 1138 and 1871 of the Social Security Act (42 U.S.C. 1302, 1306, 1320b-8 and 1395hh); and section 301 of the National Organ Transplant Act, as amended (42 U.S.C. 274e).

2. Section 121.13 is revised to read as follows:

§ 121.13 Definition of human organ under section 301 of the National Organ Transplant Act of 1984, as amended.

“Human organ,” as covered by section 301 of the National Organ Transplant Act, as amended, means the human (including fetal) kidney, liver, heart, lung, pancreas, bone marrow and other hematopoietic stem/progenitor cells without regard to the method of their collection, cornea, eye, bone skin, and intestine, including the esophagus, stomach, small and/or large intestine, or any portion of the gastrointestinal tract.”

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