

DEPARTMENT OF HEALTH AND HUMAN SERVICES

42 CFR Part 121

RIN 0906-AA73

Organ Procurement and Transplantation Network

AGENCY: Health Resources and Services Administration, HHS.

ACTION: Notice of proposed rulemaking.

SUMMARY: This notice of proposed rulemaking sets forth the Secretary's proposal to include vascularized composite allografts, described below, within the definition of organs covered by the rules governing the operation of the Organ Procurement and Transplantation Network. The Secretary further proposes a corresponding change to the definition of human organs covered by section 301 of the National Organ Transplant Act of 1984, as amended.

DATES: To be considered, comments on this proposed rule must be submitted by February 14, 2012. Subject to consideration of the comments submitted, the Department intends to publish final regulations.

ADDRESSES: You may submit comments, identified by RIN 0906-AA73, by any of the following methods:

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

- *Agency Web site:* <http://www.hrsa.gov/>. Follow the instructions for submitting comments on the Agency Web site.

- *Email:* VCATransplantation@hrsa.gov. Include RIN 0906-AA73 in the subject line of the message.

- *Fax:* (301) 594-6095.
- *Mail:* James Bowman, M.D., Medical Director, Division of Transplantation, Healthcare Systems Bureau, Health Resources and Services Administration, 5600 Fishers Lane, Room 12C-06, Rockville, Maryland 20857.

- *Hand Delivery/Courier:* James Bowman, M.D., Medical Director, Division of Transplantation, Healthcare Systems Bureau, Health Resources and Services Administration, 5600 Fishers Lane, Room 12C-06, Rockville, Maryland 20857.

Instructions: All submissions received must include the agency name and Regulatory Information Number (RIN) for this rulemaking. All comments received will be posted without change to <http://www.hrsa.gov/>, including any personal information provided. For

detailed instructions on submitting comments and additional information on the rulemaking process, see the "Public Participation" heading of the **SUPPLEMENTARY INFORMATION** section of this document.

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: James Bowman, M.D., at the above address; telephone number (301) 443-4861.

SUPPLEMENTARY INFORMATION: The transplant community has performed transplants of hands and various body parts using the term composite tissue allograft; however, for the purposes of rulemaking, the Health Resources and Services Administration (HRSA) has defined a subset of such body parts as vascularized composite allografts (VCA), which share certain characteristics.

Based upon a review of VCA, the Secretary believes that VCA should now be included within the definition of organs covered by the rules governing the operation of the Organ Procurement and Transplantation Network (OPTN) (hereinafter the OPTN final rule) (42 CFR part 121). This notice sets forth the history of VCA transplants, the factors that have persuaded the Department of the advisability of including VCA within the authority of the regulations governing the operation of the OPTN, the Secretary's oversight of VCA, and the anticipated consequences of this proposal. The notice also discusses the Department's proposal to include VCA within the definition of human organs covered by section 301 of the National Organ Transplant Act of 1984, as amended (hereinafter section 301 of NOTA).

Public Participation

Through this notice, the Secretary seeks comments from the public on the proposals made. Additional information on the submission of comments and/or the rulemaking process can be obtained from the Director, Division of Policy Review and Coordination, Health Resources and Services Administration, 5600 Fishers Lane, Room 14A-11, Rockville, Maryland 20857.

Background

VCA transplantation comprises transplants of a variety of body parts (all of which contain similar characteristics, described later) that are not currently regulated under the OPTN final rule. Perhaps the two most notable types to date have been hand and face transplants. The first successful hand transplant in the United States was performed in 1999 and the first face transplant in the U.S. was performed in 2008. Worldwide, there have been over three dozen limb transplants, at least a dozen transplants of portions of the face, and a small number of transplants of other such anatomical parts (e.g., abdominal wall, vascularized skeletal muscle, and digits). Accurate data about the actual number of such transplants have been difficult to obtain because there is no requirement for reporting these procedures in the U.S. Most of the available information has been obtained from published news accounts in the popular press and anecdotal reports in the medical literature.

Although the body parts involved vary significantly, among their shared characteristics is the fact that they are susceptible to ischemia (damage or death from lack of blood flow) and that they need revascularization, done through a surgical reconnection of blood vessels to accomplish the transplant, as opposed to secondary ingrowth of vessels. In viable vascularized transplants, immunosuppression is necessary to prevent or treat rejection. This immunosuppression has risks, which have been justified in patients needing organs as presently defined in the OPTN final rule because of their lifesaving potential. In the past, the risks of immunosuppression have inhibited transplantation of VCA because the risks associated with the prolonged use of immunosuppressive drugs were thought to exceed the expected benefits of the transplants. However, the powerful impact these transplants can have to improve the quality of life for individuals with grievous disabilities has become increasingly apparent. Immunosuppressive management for these transplants has also improved so that risks associated with immunosuppression, such as cancer, infection, or other morbidities in recipients, are lessened considerably. (F Schuind, Hand transplantation and vascularized composite tissue allografts in orthopaedics and traumatology, *Orthopaedics & Traumatology: Surgery & Research* (2010) 96, 283-290, and Armed Forces Institute of Regenerative Medicine Annual Report, 2009, pp II-1 and II-62 and II-63). In recent years, the

Departments of Defense and Veterans Affairs have initiated substantial funding of clinical research programs for limb and face transplantation anticipating the reconstruction needs of wounded service members returning from the conflicts in Iraq and Afghanistan. More than 1,000 military men and women have lost an arm or leg in these conflicts and 20 percent have lost two or more limbs. As of mid-summer 2010, it was estimated that as many as 200 wounded troops might be eligible for face transplantation and about 50 for hand/forearm transplants. Most of the funding for limb and face transplantation research in the U.S. currently comes from the Departments of Defense and Veterans Affairs (Armed Forces Institute of Regenerative Medicine Annual Report, 2009, pp I-1 and I-2). For these reasons, it is likely that the numbers of VCA transplanted will increase in the future.

Human cells or tissue intended for implantation, transplantation, infusion, or transfer into a human recipient are regulated as a human cells, tissues, and cellular and tissue-based products or HCT/Ps. The Food and Drug Administration (FDA) regulates HCT/Ps under 21 CFR parts 1270 and 1271. Examples of such tissues are bone, skin, corneas, ligaments, tendons, dura mater, heart valves, hematopoietic stem/progenitor cells derived from peripheral and cord blood, oocytes, and semen. Face and hand allografts, and other body parts meeting the proposed definition of VCA in this notice are currently not explicitly excluded from the definition of HCT/Ps under FDA regulations and are therefore subject to FDA oversight. The FDA has no statutory or regulatory authority to mandate VCA allocation policies, direct coordination of procurement efforts, require consistent application of recovery and logistics processes, or establish mandatory outcomes reporting and provide oversight of VCA transplant programs. FDA does not regulate the transplantation of vascularized human organ transplants such as kidney, liver, heart, lung, or pancreas. The Health Resources Services Administration oversees the transplantation of vascularized human organs.

Given the anticipated increase in VCA transplants, HRSA published a Request for Information (RFI) on March 3, 2008, in the **Federal Register** for the purpose of soliciting feedback from stakeholders and the public as to whether VCA should be included within the definition of organs covered by the OPTN final rule and/or added to the definition of human organs covered by section 301 of NOTA. (73 FR 11420.)

HRSA also sought feedback on the optimal way to define VCA if either definitional change was pursued.

Through the RFI, HRSA invited the public to attend a meeting on April 4, 2008 to discuss the issues described above. The meeting was well attended and provided a venue for discussion on VCA issues. Participants were instructed to provide written comments and the deadline for these comments to be received by HRSA was extended to July 2, 2008.

In response to its RFI, HRSA received 11 written comments about whether VCA should be included within the definition of organs covered by the OPTN final rule.

Eight of the written comments received supported including VCA within the definition of organs covered under the OPTN final rule. Many of these comments included similar supporting statements for OPTN oversight. The commenters agreed that the use of the existing solid organ transplant infrastructure would ensure rapid and equitable placement of VCA; allow allocation of VCA over a wide geographic area; facilitate identification of appropriate VCA donor and recipient pairs; provide assurance that all VCA programs are following similar rules, ensuring uniform and appropriate clinical and ethical standards on both the donation and transplantation side; facilitate the development of expertise and a body of knowledge that would be a valuable resource to address questions from the government or the public, and in the development of future policy and procedures in the field of VCA transplantation; enhance public transparency, increasing public acceptance of donation of VCA; and facilitate the protection of public health and safety in the context of VCA transplantation. Commenters also stated that the structure and goals of the OPTN are well aligned with the types of clinical and ethical concerns raised by VCA transplantation such as contingency treatment plan for complete face graft loss and fear of loss of facial identity due to transfer of donor facial characteristics (AJ Alexander *et al*, Arguing the Ethics of Facial Transplantation, Arch Facial Plast Surg. 2010;12(1):60-63) and with the types of entities that would be carrying out these activities, e.g., organ procurement organizations (OPOs) and transplant centers.

Of the three remaining comments, two supported partial inclusion of VCA within the OPTN final rule's definition of organs and the third comment did not support having VCA included within the OPTN final rule's definition of

organs. Of the two comments advocating partial inclusion of VCA under the OPTN final rule's definition of organs, one stated that VCA should be classified as either "life extending" or "not life extending." Life extending VCA were described as those involving: (a) Vascularized tissue, such as the use of abdominal wall transplanted to close a ruptured wound in a small bowel transplant recipient; and (b) non-vascularized tissue, such as a heart valve. Not life extending VCA were described as those involving: (c) vascularized tissue, such as a hand transplant; and (d) non-vascularized tissue, such as an anterior cruci, bone, or nerve grafts. The commenter supported including "life extending" VCA (a and b in the above examples) under the definition of organs under the OPTN final rule. According to this commenter, all life-saving VCA should follow the same rigorous testing and screening of donors and the procurement that is currently conducted by the OPTN contractor for organs currently covered under the OPTN final rule. However, the responder strongly opposed regulating "not life extending" VCA (c and d in the above examples), which are not conventional organ grafts, under the OPTN final rule. The responder suggested that although the OPTN should regulate control of distribution of the grafts, these two "not life extending" types (c and d) should be subject to less oversight. The commenter recommended new oversight legislation that would not hamper the innovation and utilization of these novel types of VCA. The Secretary wishes to make clear that certain of the body parts discussed by this commenter (e.g., non-vascularized tissues, such as heart valves and anterior cruci, bone, or nerve grafts, regardless of whether they would be considered life-saving or life-enhancing) are regulated by the Food and Drug Administration (FDA) as HCT/Ps. (21 CFR part 1271).

The second comment supported limited oversight of VCA by the OPTN at this time. The commenter supported OPTN oversight with respect to designation of VCA transplant programs, data submission regarding transplant procedures, and donor screening. However, the commenter does not support allocation policies for VCA at this time due to the unknown clinical demand and overall future of these transplants. As noted above, clinical demand for VCA transplantation appears to be increasing now that immunosuppression protocols have proven safer and support for

military and veterans VCA transplantation programs continues to expand. The issues concerning allocation, recipient safety, and outcomes reporting are similar for VCA and for organs currently under the OPTN's auspices. The VCA transplant community has clearly indicated its support for Federal oversight of VCA as organs through the OPTN in a letter of request from the Association of Organ Procurement Organizations to the Assistant Secretary of Health (December 9, 2010) and a publication of recommendations by the American Society of Transplant Surgeons in 2011 (Implementation of Vascularized Composite Allografts in the United States, *American Journal of Transplantation* (2011) 11:13–17).

The third comment did not support including VCA within the OPTN final rule's definition of organs. The comment stated that VCA do not fit as organs under HRSA oversight due to differences between solid organs procured for transplantation with the intent to save lives and VCA that are not used in life-saving applications. It also stated that the regulations that govern organ donation and transplantation are designed to maximize donation and to provide organs to as many waiting-list recipients as possible to avoid death due to their medical illness. According to the commenter, VCA recipients should not be subject to the same risks of donor transmissible diseases as recipients of traditional solid organs (e.g., heart, lung, liver, and kidney). The commenter suggests that human-derived graft materials which enhance lives can be designated by Federal regulations under oversight of FDA as either an HCT/P, a biologic, or a medical device. However, both traditional organs and VCA originate from the same pool of potential donors and therefore subject all of these transplant recipients to similar risks of donor transmissible diseases. As described elsewhere, VCA share anatomic, clinical, allocation-logistical characteristics more closely related to those of traditional organs than biologics or medical devices. Therefore, in the Secretary's view, the appropriate way to distinguish those body parts that should be regulated as organs under the OPTN final rule and those that should not be similarly defined is based upon the properties of the body parts themselves rather than whether the intent is considered life-saving or life-enhancing. The OPTN final rule does allow some flexibility specific to each organ such that the OPTN may develop distinct organ-specific policies tailored to the

circumstances, including risk of donor transmissible disease by transplanting particular organs.

The Secretary has considered comments that VCA such as hand transplants are not life saving and therefore are different from organs presently under HRSA and OPTN oversight. The Secretary does not agree with a direct demarcation between life-saving organ transplants and life-enhancing organ transplants for the purposes of defining organs under the OPTN final rule. The kidney has always been included in the list of organs governed by NOTA, the OPTN final rule, and the OPTN. Until additional life years provided by a kidney transplant (as opposed to continuing dialysis) were demonstrated, a kidney transplant was not understood to be life-saving. This fact did not dissuade the Congress from determining that kidneys should be subject to oversight under NOTA at its original enactment in 1984. As a result, kidney transplants are under the purview of the OPTN final rule and the OPTN (and subject to oversight by HRSA). Moreover, instead of adopting an all or nothing approach (life-extending versus life-enhancing), it may be better to understand improvements to the quality of life and increases to the length of life as coexisting on a spectrum of benefits. Hand and face transplants, and transplants of other body parts qualifying as VCA under the definition proposed here, may prove to be more powerful in improving a recipient's quality and extension of life than previously understood. In the Secretary's view, the appropriate way to distinguish between those VCA that should be regulated as organs under the OPTN final rule and body parts that should not be similarly defined is based upon the properties of the body parts themselves, rather than their potential impact upon the lives of their recipients.

Upon consideration of the comments received, and for the reasons described below, the Secretary now proposes that transplants of VCA be regulated under the OPTN final rule and governed by section 301 of NOTA.

Adding VCA to the Definition of Organs Covered by the OPTN Final Rule

Through this notice, the Department proposes adding VCA to the definition of organs included in the OPTN final rule, codified at 42 CFR 121.2, through rulemaking. When it enacted NOTA in 1984, Congress included a definition of the term organ and authorized the Secretary to expand this definition by regulation. The Secretary has previously exercised this authority and expanded

the statutory definition of organ. Currently, the OPTN final rule defines covered organs as "a human kidney, liver, heart, lung, or pancreas, or intestine (including the esophagus, stomach, small and/or large intestine, or any portion of the gastrointestinal tract). Blood vessels recovered from an organ donor during the recovery of such organ(s) are considered part of an organ with which they are procured for purposes of this part if the vessels are intended for use in organ transplantation and labeled 'For use in organ transplantation only.'"

One of the major reasons NOTA was enacted and affirmed by several amendments was to establish an organ allocation system that functions equitably on a nationwide basis with provisions for outcomes reporting and evaluation. Prior to the enactment of NOTA, deceased donor organs were allocated regionally, based on relationships between transplant programs and donor hospitals. Congress recognized the need to allocate this national resource on a national and equitable basis. To ensure equitable access for those awaiting VCA transplantation, there is a need to provide for consistency in allocation processes and reliable outcomes reporting on a nationwide basis. Appropriate Federal oversight of a national allocation system can increase safety of such transplants and provides equitable and consistent national access to such transplants while also conveying to the public that donation for such purpose will serve an essential medical need. The FDA does not have statutory authority to provide oversight of VCA allocation, outcomes reporting, or promotion of donation. The Secretary believes that the rationale for a national system of organ allocation and outcomes reporting underlying NOTA applies to VCA.

Once a body part is defined as an organ under the OPTN final rule, such body parts are excluded from the coverage of FDA regulations governing HCT/Ps. In addition, transplants involving body parts defined as organs under the OPTN final rule are subject to the requirements of the OPTN final rule. For example, entities performing transplants with covered organs must receive designation as an organ-specific designated transplant program (in this case, a designation as a VCA-specific transplant program) within an OPTN member institution. Members must comply with data submission requirements of the OPTN final rule and are subject to oversight by the OPTN contractor for compliance with OPTN policies, OPTN bylaws, and the OPTN

final rule. Members may be subject to Federal enforcement actions for violations of Federal regulations or enforceable policies (those approved by the Secretary of Health and Human Services) or for actions or inactions that indicate a risk to health of patients or to the public safety. Finally, OPTN members can be subject to OPTN sanctions for violating OPTN bylaws and non-enforceable OPTN policies (e.g., being declared a member not in good standing).

As previously discussed and also explained in “Statement of Need” within the “Impact of the New Rule” section (below), the Secretary believes that oversight of the VCA transplants is necessary to ensure transplant recipient safety and to provide a consistent allocation process nationwide that will ensure equitable access to those waiting for VCA transplantation., to collect data on VCA transplant outcomes, and to maintain the public trust in the integrity of the VCA donation, recovery and transplant processes. Because of the clinical, procurement, logistical, allocation, and outcomes reporting similarities between VCA and organs currently under the OPTN’s auspices, the Secretary believes that HRSA is the appropriate HHS agency to assure Federal oversight over VCA transplantation. HRSA oversees transplantation of vascularized human organs through the OPTN, which sets policies related to the procurement, transplantation, allocation, and outcomes reporting of human organs. The OPTN serves the critical role of matching donor organs to potential recipients on a national basis. The issues concerning allocation and recipient safety are similar for VCA and for organs currently under the OPTN’s auspices. Additionally, the membership of the OPTN, which is charged with developing policies consistent with the OPTN final rule, includes professionals with expertise in the field. Therefore, the Secretary believes that the OPTN, with HRSA’s oversight, will be able to effectively address issues involving the regulation of the emerging field of VCA transplantation.

If VCA are included within the OPTN final rule’s definition of organs, transplants involving VCA will be subject to the requirements of the OPTN final rule. For example, an entity performing VCA transplants would have to receive designation as a VCA-designated transplant program within an OPTN member institution. In addition, OPTN members would be required to comply with the OPTN final rule’s data submission requirements with respect to the transplants

performed. Thus, the OPTN would need to devise certain policies with respect to VCA, including allocation policies meeting the requirements set forth in the OPTN final rule. Finally, OPTN members would be subject to oversight by the OPTN contractor for compliance with OPTN policies extending to VCA (e.g., those concerning donor screening and allocation), and could be subject to enforcement actions for violations of such policies.

Even so, the OPTN final rule does allow some flexibility specific to each organ. The OPTN sometimes fashions distinct organ-specific policies tailored to the circumstances of transplanting particular organs. For example, the training of professionals working for designated programs may vary by organ and OPTN policies with respect to disease transmission protocols and testing may diverge based on circumstances relating to particular organs. Likewise, the particular characteristics of and circumstances surrounding different types of organs lead to different OPTN allocation policies.

In addition, if VCA are added as covered organs under the OPTN final rule as proposed here, the Secretary will continue to exercise oversight over proposed and final OPTN policies with respect to VCA, consistent with the authority of the Secretary under 42 CFR 121.4. Given the relatively small numbers of other VCA transplanted at this time, the Secretary does not expect that the OPTN would develop allocation policies for all VCA within a short time frame if VCA are added to the OPTN final rule’s definition of organs. We expect that the OPTN will initially create policies addressing hands and faces as these two VCA have been the most frequently performed VCA transplant procedures in the U.S. and are the subject of extensive ongoing clinical research programs by the Departments of Defense and Veterans Affairs. We expect that the OPTN will wait to develop allocation policies for other VCA until the field has more clinically evolved. Given the Secretary’s substantial interest in VCA policy and involvement in the operations of the OPTN, the Secretary will be notified of proposals to develop policies for other VCA as they are addressed in the future.

The nature of the regulatory framework governing the operation of the OPTN underlies the importance of including VCA within the definition of organs covered by the OPTN final rule. Under the OPTN final rule, the OPTN must submit proposed policies for review and approval by the Secretary (42 CFR 121.4). Upon consideration of

public comments on proposed policies that are considered significant, the Secretary will determine whether to make such proposed policies enforceable in accordance with section 121.10 of the OPTN final rule. The Secretary may direct the OPTN to develop individual policies for specific body components that are defined as VCA in addition to OPTN policies that apply to all VCA. Any transplant hospital that fails to comply with any policy approved as enforceable by the Secretary under this process may be subject to the enforcement sanctions delineated in section 121.10 of the OPTN final rule, including possible termination from the Medicare and Medicaid programs.

The Secretary has the following additional authorities provided by the OPTN final rule (42 CFR 121.4(b)(2)), which she may exercise in the case of policies extending to VCA: The Secretary may require the OPTN Board of Directors to provide to the Secretary, at least 60 days prior to their proposed implementation, proposed policies on matters that the Secretary directs. The Secretary will refer significant proposed policies to the Advisory Committee on Organ Transplantation (ACOT) established under 42 CFR 121.12, and publish them in the *Federal Register* for public comment. This is in addition to the public comment process that is engaged in by the OPTN.

The Secretary also may seek the advice of the ACOT on other proposed policies and publish them in the **Federal Register** for public comment.

The Secretary will determine whether proposed policies are consistent with NOTA and the OPTN final rule, taking into account the views of the ACOT and public comments. Based on this review, the Secretary may provide comments to the OPTN.

If the Secretary concludes that a proposed policy is inconsistent with NOTA or the OPTN final rule, the Secretary may direct the OPTN to revise the proposed policy consistent with the Secretary’s direction. If the OPTN does not revise the proposed policy in a timely manner, or if the Secretary concludes that the proposed revision is inconsistent with NOTA or the OPTN final rule, the Secretary may take such other action as the Secretary determines appropriate, but only after additional consultation with the ACOT on the proposed action.

Also, the Secretary has the authority under the OPTN Final Rule (42 CFR 121.4(a)(6)) to require the OPTN to develop policies on such matters as the Secretary directs.

The Secretary is legally obliged, as part of her responsibilities in administering the Medicare and Medicaid programs, to require hospitals that transplant organs to comply with the rules and requirements of the OPTN as a condition of their participation in Medicare and Medicaid. (42 U.S.C. 1320b–8(a)(1)(B).) Because VCA are not included within the OPTN final rule's definition of organs, the Secretary could not currently make any VCA allocation policy enforceable. If VCA are added as covered organs under the OPTN final rule as proposed here, the Secretary could take appropriate enforcement actions against an OPO or transplant hospital for failing to comply with the OPTN's VCA retrieval and allocation policy, if such a policy has been approved as enforceable by the Secretary under the process outlined above. If VCA are defined as organs under the OPTN final rule, then this will ensure that VCA organ allocation, whether pertaining to isolated VCA transplants or combined/multi-organ transplants, is consistent with OPTN final rule's goals, including that of an equitable national system for organ allocation, to be consistent with NOTA.

Even if OPTN policies pertaining to VCA transplantation do not become enforceable, all institutions performing VCA transplantation would be required to comply with the provisions of the OPTN final rule (including the requirement that such institutions become members of the OPTN). Further, such institutions could be subject to sanctions by the OPTN for failure to comply with allocation and other OPTN policies. For example, a member may be named a member not in good standing by the OPTN for failing to comply with such a policy.

As the field of VCA transplantation evolves, it will become more critical that VCA organ allocation keeps pace with advances in the field; that the field be subject to appropriate Federal oversight; that policy developments include performance indicators to assess whether the goals of an equitable transplant system are being achieved; that the Secretary have the authority to make those policies enforceable; and that patients and physicians have timely access to accurate data that will assist them in making decisions regarding VCA transplantation. Upon consideration of the foregoing factors, and to achieve the most equitable and medically effective use of donated organs, the Secretary proposes that VCA should explicitly be added to the definition of organs covered by the OPTN final rule. The Secretary seeks comments on this proposal.

Defining Vascularized Composite Allografts

At the time of the RFI, and to assist the Secretary in adding VCA to the definition of organs covered by the OPTN final rule and/or to the definition of human organs governed by section 301 of NOTA, HRSA sought feedback from stakeholders and from the public as to how such allografts should be defined. HRSA identified two potential approaches: (1) A broad regulatory definition describing the common features of VCA without listing covered body parts; or (2) a definition listing body parts that would qualify as VCA.

The Secretary has elected to propose the first approach, a broad regulatory definition that describes the features of the allografts without listing particular body parts. Under this approach, the definition would extend to transplants of particular body parts that are not known to have been performed clinically to date, or even to body parts whose transplantation has not yet been envisioned. The Secretary is proposing which elements should be included in the definition of VCA to be sufficiently broad to cover the universe of intended body parts, but narrow enough to put the public on notice as to which parts meet the regulatory definitions of organs.

The Secretary proposes that for a body part to be defined as a VCA, it must have all the following characteristics: a body part (1) That is vascularized and requires blood flow by surgical connection of blood vessels to function after transplantation; (2) containing multiple tissue types; (3) recovered from a human donor as an anatomical/structural unit; (4) transplanted into a human recipient as an anatomical/structural unit; (5) minimally manipulated, (processing that does not alter the original relevant characteristics of the organ relating to the organ's utility for reconstruction, repair, or replacement—examples of minimal manipulation include cutting, grinding, and shaping of a VCA); (6) for homologous use, (the replacement or supplementation of a recipient's organ with an organ that performs the same basic function or functions in the recipient as in the donor), (e.g., a hand from the donor is to be used as a hand in the recipient); (7) not combined with another article such as a device; (8) susceptible to ischemia and, therefore, only stored temporarily (e.g., cold storage in preservation medium and intended for implantation into a recipient within hours of the recovery) and not cryopreserved; and (9) susceptible to allograft rejection,

requiring immunosuppression that may increase infectious disease risk to the recipient. This proposed definition is intended to explain to the public which body parts would be covered presently, while allowing other body parts that are transplanted to be covered as the field of VCA transplantation advances. A non-exclusive list of body parts that would meet the proposed definition for VCA here would include faces, hands, fingers, toes, larynges, and abdominal walls. Periodically, HRSA may publish an updated list of VCA in the *Federal Register*. In addition, through this definition, the Secretary intends to distinguish those body parts she proposes to define as organs under the OPTN final rule from other body parts that are regulated as HCT/Ps under FDA's regulatory authority.

Under a second alternative, the Secretary could have proposed a definition that lists specific transplantable body parts to be added to the definition of organs (e.g., face, hand, etc.). The Secretary finds this unnecessary since the general set of nine characteristics provide clear identification of such body parts. Moreover, definition by an explicit list would likely exclude certain body parts for which transplantation might be possible, but not done to date (either in the United States or internationally). The Secretary is proposing the more descriptive definition to avoid the need of amending the regulatory definition to extend its reach to new types of transplantation that emerge in the future.

HRSA received no negative feedback in response to its request for information on adopting this first approach or on the criteria discussed in the request for information (other than the comment distinguishing between those grafts that are lifesaving and those that are life enhancing). Most of the commenters supporting the inclusion of VCA in the definition of organs covered by the OPTN final rule would defer to the physicians and surgeons involved to determine the optimal way to define VCA. Given that Congress authorized the Department to modify the definition of covered organs through rulemaking, it would not be permissible to allow transplant surgeons and physicians (or others participating in the OPTN), on their own, to define VCA for the purposes of the final rule. However, the Secretary seeks feedback from the transplant community on the definition of VCA proposed here.

Additionally, body parts allocated as VCA are intended to be used "intact" as a VCA until the transplant center receiving the VCA determines that a

portion of the VCA is not needed for transplantation of the remainder of the VCA. If portions of a VCA are not used in connection with the same transplant (for example, left over bone or tendons from a limb allocated as a VCA), such body parts cannot be used for other purposes including transplantation in a different anatomical location in the recipient who received the VCA or in a different recipient. Disposition of such remnants would be subject to OPTN policies.

Because the Secretary is proposing a definition that does not identify specific VCA by name, the Secretary proposes amending 42 CFR 121.4(e) to make clear that the OPTN must identify the specific body parts covered by any OPTN policy specific to VCA. The purpose of this proposal is to ensure that all OPTN members and stakeholders understand the body parts covered by OPTN policies specific to VCA. Under this proposal, any OPTN policy that applies broadly to organs would apply to all body parts meeting the proposed definition for VCA unless otherwise provided for.

State registries for organ and tissue donors generally provide the option to select organs, tissues, both, or neither. In the future we anticipate that states will likely further distinguish VCAs and will continue to permit individuals to select what they wish to donate. The potential impact of including VCA in the definition of organs on organ donation efforts, including the number of deceased donor organs that may become available, has not been explored. Therefore, the Secretary is seeking public comment on what impact this proposed expanded definition of organs may have on efforts to increase participation in deceased organ donor registries, signing organ donor cards, and general willingness of individuals to agree to be deceased organ donors.

Including VCA Within the Definition of Human Organs Covered by Section 301 of NOTA

The Secretary further proposes including VCA within the definition of human organs, as covered by section 301 of NOTA, which prohibits the purchase or sale of human organs for human transplantation. This criminal prohibition provides in part that “[i]t shall be unlawful for any person to knowingly acquire, receive, or otherwise transfer any human organ for valuable consideration for use in human transplantation if the transfer affects interstate commerce. The preceding sentence does not apply with respect to human organ paired donation.” (42 U.S.C. 274e(a).) Section 301 of NOTA

defines the term “human organ” to mean “the human (including fetal) kidney, liver, heart, lung, pancreas, bone marrow, cornea, eye, bone, and skin or any subpart thereof and any other human organ (or any subpart thereof, including that derived from a fetus) specified by the Secretary of Health and Human Services by regulation.” (42 U.S.C. 274e(c)(1).)

As set forth by statute, Congress authorized the Secretary to add additional organs to the definition of human organ covered by section 301 through rulemaking to include the transplantation of additional human organs within section 301’s prohibition. The Secretary has previously exercised this authority. Adding VCA to this definition of human organs will subject persons violating its terms to VCA to criminal penalties.

Through this notice, the Secretary proposes to add VCA to the list of human organs covered by section 301 of NOTA. The Secretary proposes modifying 42 CFR 121.13, which includes the definition of human organs covered by section 301 of NOTA, to include VCA (as defined in the proposed amendment to section 121.2 of the OPTN final rule). Subparts are being added to this definition to conform with Public Law 100–607, which added subparts of covered human organs to the statutory definition of human organs governed by section 301 of NOTA.

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.

Executive Order 12866 requires that all regulations reflect consideration of alternatives, costs, benefits, incentives, equity, and available information. Regulations must meet certain standards, such as avoiding an unnecessary burden. Regulations that are significant because of cost, adverse effects on the economy, inconsistency with other agency actions, effects on the budget, or novel legal or policy issues, require special analysis.

The Secretary has determined that minimal resources are required to

implement the requirements in this rule because organizations involved (*e.g.*, OPOs and transplant hospitals) already implement related requirements for other organs in the OPTN rule (42 CFR 121.2). 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 have no 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.

As stated above, this proposed rule would modify the regulations governing the OPTN and section 301 of NOTA based on legal authority.

Impact of the New Rule

Statement of Need

The field of VCA transplantation has advanced from the first hand transplant in the U.S. in 1999 to the point that there are now more than a dozen VCA transplant centers extending from coast to coast involving hand, face, abdominal wall, larynx, and possibly other body parts. The Departments of Defense and Veterans Affairs have invested hundreds of millions of dollars in clinical VCA transplantation research programs for the benefit of wounded warriors returning from the Iraq and Afghanistan conflicts with extensive debilitating injuries of the face and multiple extremities. Although the current activity level is less than a dozen transplants a year in the U.S., the VCA transplant community has begun to encounter the expansion problems faced

in the early days of organ transplantation with ensuring equitable access for patients to VCA, uniform allocation policies across the U.S., coordination of procurement efforts, consistent application of recovery and logistics processes, and monitoring patient safety with appropriate outcomes reporting and oversight of transplant programs.

VCA transplantation consists of surgical transplants of a variety of body parts that currently do not fall within the current regulatory definition of "organ" covered by the rules governing the operation of the OPTN. Face and hand allografts, and other body parts meeting the definition of VCA in this notice, currently are subject to FDA oversight under 21 CFR parts 1270 and 1271. VCA, like organs, differ from tissues in that they must be transplanted within hours (not months or years), recipients require immunosuppression drugs to prevent or treat rejection, and the allocation process requires specific genetic and clinical matching between donor and recipient.

The FDA has no statutory or regulatory authority to mandate allocation policies, direct coordination of procurement efforts, require consistent application of recovery and logistics processes, or establish mandatory outcomes reporting and provide oversight of VCA transplant programs. In short, the FDA's authority for regulation of tissues like VCA stops at the hospital door. Only the OPTN, under HRSA oversight, can provide reliable consistent and mandatory mechanisms and infrastructure to address these problems facing the VCA transplant community. Recognizing the need for such efforts to continue to advance the field of VCA transplantation, the VCA transplant community specifically requested the Secretary of the Department of Health and Human Services to provide the necessary regulatory change to define those body parts meeting the definition of VCA in this notice as "organs" under the OPTN Final Rule so that VCA transplantation can continue to progress in an appropriate manner that will best serve the patients in need of such allografts.

This proposed rule would have the effect of including VCA within the ambit of the regulations governing the operation of the OPTN, and would include transplanted human VCA within the prohibition set forth at section 301 of NOTA. If implemented, the proposals set forth in this rule would authorize the Secretary to take enforcement actions against entities violating OPTN policies pertaining to

the transplantation of VCA once such policies are approved as enforceable by the Secretary. Even if the Secretary does not approve such policies as enforceable, OPTN members will be subject to enforcement actions by the OPTN for violations of OPTN policies extending to VCA. If this rule is promulgated, OPTN members will be required to comply with requirements set forth in the OPTN final rule, including those pertaining to data submission, as applied to VCA. Finally, if this proposal is implemented, individuals violating section 301 of NOTA with respect to VCA transplants would be subject to criminal penalties.

If this rule takes effect, transplant centers that perform VCA transplantation would be required to take the necessary steps to ensure that VCA transplant programs are in compliance with any policies enacted by the OPTN specific to designated VCA allografts (e.g. hand, face). Such policies typically specify the clinical submission requirements for candidate registration on the waiting list, clinical information of the transplant procedure, follow up reporting on graft and patient outcomes, and reporting of potential donor disease transmission events.

Paperwork Reduction Act of 1995

The amendments proposed in this notice of proposed rulemaking contain information collection activities that are very similar to, and based on the data collection requirements in, the OPTN final rule approved by the Office of Management and Budget (OMB No. 0915-0157 and OMB No. 0915-0184). Membership in the OPTN is determined by submission of application materials to the OPTN demonstrating that the applicant meets all required criteria for membership and will agree to comply with all applicable provisions of the National Organ Transplant Act, as amended, 42 U.S.C. 273 *et seq.* Section 1138 of the Social Security Act, as amended, 42 U.S.C. 1320b-8 requires that hospitals in which transplants are performed be members of, and abide by, the rules and requirements (as approved by the Secretary of the HHS) of the OPTN as a condition of participation in Medicare and Medicaid for the hospital. Section 1138 contains a similar provision for the organ procurement organizations (OPOs) and makes membership in the OPTN and compliance with its operating rules and requirements (as approved by the Secretary of the HHS), including those relating to data collection, mandatory for all transplant programs and OPOs. The information is used predominantly to match donor organs with recipients,

to monitor compliance of member organizations with OPTN policies and requirements to guide organ allocation policy development, and to report periodically on the clinical and scientific status of organ donation and transplantation in this country.

The currently-approved data collection includes worksheets and burden for organs and describes respondents as non-profit institutions and small organizations, which would be the same for this proposed rule. The title, description, and respondent description of all information collections relating to VCA are shown below with similar estimates of annual reporting and record keeping burden as with other organs previously approved in the OPTN final rule.

Currently there are approximately 10 hand, 2 face, and 1 abdominal wall transplant programs in the U.S., although only 7 have actually performed a clinical transplant operation to date. Since the current rate of VCA transplants is less than 10 a year (hand) and less than 1 a year (face and abdominal wall), for reporting burden calculations (below) we have projected a total of 20 VCA transplant programs each registering 2 candidates a year to the waiting list and each program performing 1 transplant procedure a year. The data burden calculation in the table below assumes that data associated with entering deceased donor information is already accounted in the current OMB approved data collection forms. Specifically, it is reasonable to assume that any donor that would be considered as a VCA donor is also considered to be a donor for other organs covered by this rule. The hourly rate used for calculation of total burden cost to respondents is the average hourly wage for a transplant data coordinator (\$26.00). This rate reflects the median annual salary and benefits for a Data Control Clerk II (www.salary.com) The total annual respondent burden hours (202) represents 10.1 hours (\$262.60) per respondent.

Title: Organ Procurement and Transplantation Network.

Description: Information will be collected from transplant hospitals, organ procurement organizations, and histocompatibility laboratories predominantly for the purpose of matching donor VCA with potential recipients, monitoring compliance of member organizations with system rules, conducting statistical analyses, and developing policies relating to organ procurement and transplantation.

The practical utility of the data collection is further enhanced by

requirements that the OPTN must report a variety of data to the Secretary, including data on performance by organ and status category, including program-specific data, OPO specific data, data by program size, and data aggregated by organ procurement area, OPTN region, the nation as a whole, and other geographic areas (42 CFR 121.8(c)(3)). The OPTN must also transmit proposed allocation policies and performance indicators which will be used to assess the likely effects of policy changes and to ensure that the proposed policies are consistent with the OPTN final rule.

The OPTN and Scientific Registry must make available to the public timely and accurate information concerning the performance of transplant programs, and must respond to requests from the public for data needed for bona fide research or analysis purposes or to assess the performance of the OPTN or Scientific Registry, to assess individual transplant programs, or for other purposes (42 CFR 121.11(b)(1)(C)).

The OPTN must provide to each member OPO and transplant hospital the plans and procedures for reviewing

applications and for monitoring compliance with these rules and OPTN policies. The OPTN must also report to the Secretary on OPOs and transplant hospitals that may not be in compliance with these rules or OPTN policies, and on their progress toward compliance.

The OPTN and Scientific Registry are required to maintain and manage the information on candidates, donors and recipients.

Description of Respondents: Non-profit institutions and small organizations. The estimated annual reporting burden is as follows:

Section	Form	Number of respondents	Responses per respondent	Total responses	Average hours per response	Total burden hours/cost (\$)
121.6(c)	Establishing Criteria for VCA Acceptance	20	1	20	0.5	10 \$260.00
121.7(b)(4)	Reasons for Refusal	20	50	1000	0.1	100 \$2,600.00
121.9(b)	Designated Transplant Program Requirements.	20	1	20	2.0	40 \$1,040.00
121.11(b)(2) ..	Recipient Histo-compatibility	20	1	20	0.2	4 \$104.00
	VCA Candidate Registration	20	2	40	0.5	20 \$520.00
121.11(b)(2) ..	VCA Recipient Registration	20	1	20	0.75	15 \$390.00
121.11(b)(2) ..	VCA Follow-Up	20	1	20	0.65	13 \$338.00
Total	20	1,140	0.18	202 \$5,252.00

List of Subjects in 42 CFR Part 121

Health care, Hospitals, Organ transplantation, Reporting and recordkeeping requirements.

Dated: August 18, 2011.

Mary Wakefield,

Administrator, Health Resources and Services Administration.

Approved: September 7, 2011.

Kathleen Sebelius,

Secretary.

Accordingly, 42 CFR part 121 is proposed to be amended as set forth below:

PART 121—ORGAN PROCUREMENT AND TRANSPLANTATION NETWORK

1. The authority citation for part 121 continues to read as follows:

Authority: 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).

§ 121.2 [Amended]

2. Amend § 121.2 to revise definition for Organ and add definition for

Vascularized composite allograft to read as follows:

* * * * *

Organ means a human kidney, liver, heart, lung, pancreas, intestine (including the esophagus, stomach, small and/or large intestine, or any portion of the gastrointestinal tract), or vascularized composite allograft (defined in this section). Blood vessels recovered from an organ donor during the recovery of such organ(s) are considered part of an organ with which they are procured for purposes of this part if the vessels are intended for use in organ transplantation and labeled “For use in organ transplantation only.”

* * * * *

Vascularized composite allograft means a body part:

(1) That is vascularized and requires blood flow by surgical connection of blood vessels to function after transplantation;

(2) Containing multiple tissue types;

(3) Recovered from a human donor as an anatomical/structural unit;

(4) Transplanted into a human recipient as an anatomical/structural unit;

(5) Minimally manipulated, (processing that does not alter the

original relevant characteristics of the organ relating to the organ’s utility for reconstruction, repair, or replacement);

(6) For homologous use, (the replacement or supplementation of a recipient’s organ with an organ that performs the same basic function or functions in the recipient as in the donor);

(7) Not combined with another article such as a device;

(8) Susceptible to ischemia and, therefore, only stored temporarily and not cryopreserved; and

(9) Susceptible to allograft rejection, requiring immunosuppression that may increase infectious disease risk to the recipient.

3. In § 121.4, add paragraph (e)(3) to read as follows:

§ 121.4 OPTN policies: Secretarial review and appeals.

* * * * *

(e) * * *

(3) identify all covered body parts in any policies specific to vascularized composite allografts, defined in § 121.2.

4. Revise § 121.13 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 of 1984, as amended, means the

human (including fetal) kidney, liver, heart, lung, pancreas, bone marrow, cornea, eye, bone, skin, intestine (including the esophagus, stomach, small and/or large intestine, or any portion of the gastrointestinal tract), or

any vascularized composite allograft defined in § 121.2. It also means any subpart thereof, including that derived from a fetus.

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