Establishment Registration: General Information

The Food and Drug Administration (FDA) requires registration of establishments that manufacture human cells, tissues, and cellular and tissue-based products (HCT/Ps). Manufacture means, but is not limited to, any or all steps in the recovery (collection), processing (such as sterility testing), storage, labeling, packaging or distribution of any human cell or tissue, and the screening or testing for evidence of infectious disease in the tissue donor. Registration is a notice to the FDA of the list of products a facility manufactures and distributes within or to the U.S. It also provides the information FDA uses to contact establishments.

The FDA has the authority to inspect registered facilities. The inspection will cover all products that are listed in the registration. Facilities in the United States must list all HCT/Ps that are manufactured at their facility.

For international facilities, registration only applies to products that are exported to the United States. Therefore, international facilities should only list the products that may enter the U.S. regardless of any other HCT/Ps manufactured at their facility. This serves to focus the scope of an FDA inspection to activities relating to the HCT/Ps entering the United States. For international partners, listing additional products that will not be exported to the U.S. has the potential to increase the likelihood of an FDA inspection.

NMDP Network centers that are required to complete establishment registration and listing with the FDA include U.S. and international:

- donor centers
- apheresis centers
- cord blood banks

If an establishment relies on services from other organizations, these organizations may also complete establishment registration and listing with the FDA, such as:

- laboratories performing infectious disease testing (U.S. only)
- laboratories performing bacterial and fungal cultures on hematopoietic stem cells (register as processing)

**Time Requirements for Registration:**

- New establishments must register within 5 days of beginning operations or within 5 days of beginning to export HCT/Ps to the U.S.
- Registered establishments must update their registration annually in December even if there are no changes to an establishment's HCT/P listing.
- Registered establishments need to submit changes to their product listing within 6 months of the change (21 CFR 1271.21).
- If the ownership or location of the establishment changes, the establishment must amend registration information within 5 days of the change (21 CFR 1271.26).
- If a registered facility fails to submit annual renewal, it is a violation of the regulations and that facility would be subject to FDA compliance action and possible fines. Also, failure of an international establishment to register could prohibit or delay entry of a product into the U.S.
Manufacturing Activities:

The following activities meet the definition of manufacturing. Definitions for each function may include but are not limited to:

1. **Recover (collection):** collection of cells or tissues from a human donor by apheresis or collection of umbilical cord blood

2. **Screen:** screening a cell or tissue donor by review of relevant medical records for risk factors for, and clinical evidence of, relevant communicable disease or disease agents

3. **Test:** perform infectious disease testing on a donor using FDA approved donor test kits at a laboratory certified under CLIA or equivalent requirements as determined by CMS

4. **Package:** placing product in bag and packaging for shipment

5. **Process:** any activity performed on an HCT/P, other than recovery, donor screening, donor testing, storage, labeling, packaging, or distribution, such as sterility testing, sterilization, steps to inactivate or remove adventitious agents, preservation for storage, and removal from storage

6. **Store:** holding the product for future processing and/or distribution

7. **Label:** applying labels to products, or management of labels or accompanying materials about the product or the contents

8. **Distribute:** any conveyance or shipment (including importation and exportation) of an HCT/P that has been determined to meet release criteria

The chart illustrating the eight establishment functions for registration with the FDA and which facilities *typically* perform these functions in the NMDP Network:

<table>
<thead>
<tr>
<th>Establishment</th>
<th>Recover</th>
<th>Screen</th>
<th>Test</th>
<th>Package</th>
<th>Process</th>
<th>Store</th>
<th>Label</th>
<th>Distribute</th>
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<tbody>
<tr>
<td>Apheresis Center</td>
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<td>X</td>
<td>X</td>
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<tr>
<td>Donor Center</td>
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<tr>
<td>Cord Blood Bank</td>
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<td>Sterility Testing Laboratory</td>
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<td><strong>Laboratory for IDMs</strong></td>
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* Establishment functions may vary from center to center depending upon the operation as it relates to NMDP business or non-NMDP business or agreements in place with other entities.

** Laboratories that perform testing for IDMs must complete establishment registration and listing with the FDA as well; however, the center using the laboratory is responsible for ensuring that the laboratory has completed the registration. U.S. laboratories performing IDM eligibility testing per FDA requirements must complete registration; however most international laboratories do not use FDA approved IDM donor testing kits, and therefore seldom register.
Product Categories:

1. **HCT/Ps described in 21 CFR 1271.10:** This category is for autologous or first or second degree related allogeneic donations. Some facilities recover products that meet this category.

2. **HCT/Ps regulated as Medical Devices:** Does not pertain to NMDP’s work.

3. **HCT/Ps regulated as drugs or biological drugs:** The FDA regulations identify the products from unrelated allogeneic donors manufactured for the NMDP as “biological drugs.” All NMDP network establishments would indicate Peripheral Blood Stem Cell products, Therapeutic Cells, or Umbilical Cord Blood Stem Cells, as applicable, and mark this category.

**Donor Information:**

Most products manufactured for the NMDP are from allogeneic donors. Some products may be from first or second degree relatives of the intended recipient. A facility may manufacture products that fall under more than one category. For centers located in the United States, identify all products that apply. International centers should indicate only those products that will be exported to the U.S. (For example: an international facility manufactures autologous products, but none of those products are exported to the U.S. through NMDP. Those products should not be listed with the FDA in the Establishment Registration.)

**U.S. Agent:**

A U.S. Agent is required for international establishments only. Official communications between the FDA and an international facility makes use of the U.S. Agent.

The U.S. Agent provides the FDA with a contact should U.S. Customs have a question about a product that has arrived at a U.S. port of entry. The U.S. agent also serves as the U.S. contact for an international establishment if the FDA chooses to inspect that international center.

At this time, international establishments that provide products for export to the U.S. only through the NMDP may identify Dr. John Miller as the U.S. Agent. If a facility exports additional products to the U.S. outside of the NMDP, someone other than Dr. John Miller must be identified as the U.S. Agent. Also, if a facility has named Dr. John Miller as their U.S. Agent, a copy of the validated registration form must be sent to the NMDP. See the NMDP contact staff listed at the end of this document.

Refer to the “Establishment Registration Tool: Electronic Completion of eHCTERS” (Attachment #: A00456) for step-by-step instructions for completing the electronic Establishment Registration.

**References:**

**FDA Tissue Registration:**

http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/EstablishmentRegistration/TissueEstablishmentRegistration/

**FDA: Tissues and Tissue Products:**

http://www.fda.gov/BiologicsBloodVaccines/TissueTissueProducts/default.htm

**FDA Tissue Registration Coordinator:** tissue@fda.hhs.gov, phone: (301) 827-6176

**NMDP Contact:**

Lori Hanley, Regulatory Compliance: lhanley@nmdp.org, phone: (763) 406-8403

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