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SOURCE: 66 FR 5466, Jan. 19, 2001, unless otherwise noted.

Subpart A—General Provisions

§ 1271.1 What are the purpose and scope of this part?

(a) *Purpose.* The purpose of this part, in conjunction with §§ 207.9(a)(5), 210.1(c), 210.2, 807.20(d), and 820.1(a) of this chapter, is to create an electronic registration and listing system for establishments that manufacture human cells, tissues, and cellular and tissue-based products (HCT/P's) and to establish donor-eligibility, current good tissue practice, and other procedures to prevent the introduction, transmission, and spread of communicable diseases by HCT/P's.

(b) *Scope.* (1) If you are an establishment that manufactures HCT/P's that are regulated solely under the authority of section 361 of the Public Health Service Act (the PHS Act), this part requires you to register and list your HCT/P's with the Food and Drug Administration's (FDA's) Center for Biologics Evaluation and Research and to comply with the other requirements contained in this part, whether or not the HCT/P enters into interstate commerce. Those HCT/P's that are regulated solely under the authority of section 361 of the PHS Act are described in § 1271.10.

(2) If you are an establishment that manufactures HCT/P's that are regulated as drugs, devices and/or biological products under section 351 of the PHS Act and/or the Federal Food, Drug, and Cosmetic Act, §§ 207.9(a)(5) and 807.20(d) of this chapter require you to register and list your HCT/P's following the procedures in part 207 (if a drug and/or biological product) of this chapter or part 807 (if a device) of this chapter. Sections 210.1(c), 210.2, 211.1(b), and 820.1(a) of this chapter require you to comply with the donor-eligibility procedures in subpart C of this part and the current good tissue practice procedures in subpart D of this part, in addition to all other applicable regulations.

[66 FR 5466, Jan. 19, 2001, as amended at 69 FR 29829, May 25, 2004; 81 FR 60223, Aug. 31, 2016]

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

The following definitions apply only to this part:

(a) *Autologous use* means the implantation, transplantation, infusion, or transfer of human cells or tissue back into the individual from whom the cells or tissue were recovered.

(b) *Establishment* means a place of business under one management, at one general physical location, that engages in the manufacture of human cells, tissues, and cellular and tissue-based products. ''Establishment'' includes:

(1) Any individual, partnership, corporation, association, or other legal entity engaged in the manufacture of human cells, tissues, and cellular and tissue-based products; and

(2) Facilities that engage in contract manufacturing services for a manufacturer of human cells, tissues, and cellular and tissue-based products.

(c) *Homologous use* means the repair, reconstruction, replacement, or supplementation of a recipient's cells or tissues with an HCT/P that performs the same basic function or functions in the recipient as in the donor.

(d) *Human cells, tissues, or cellular or tissue-based products (HCT/Ps)* means 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/Ps include, but are not limited to, bone, ligament, skin, dura mater, heart valve, cornea, hematopoietic stem/progenitor cells derived from peripheral and cord blood, manipulated autologous chondrocytes, epithelial cells on a synthetic matrix, and semen or other reproductive tissue. The following articles are not considered HCT/Ps:

(1) Vascularized human organs for transplantation;

(2) Whole blood or blood components or blood derivative products subject to listing under parts 607 and 207 of this chapter, respectively;

(3) Secreted or extracted human products, such as milk, collagen, and cell factors; except that semen is considered an HCT/P;

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(4) Minimally manipulated bone marrow for homologous use and not combined with another article (except for water, crystalloids, or a sterilizing, preserving, or storage agent, if the addition of the agent does not raise new clinical safety concerns with respect to the bone marrow);

(5) Ancillary products used in the manufacture of HCT/P;

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

(7) In vitro diagnostic products as defined in §809.3(a) of this chapter.

(8) Blood vessels recovered with an organ, as defined in 42 CFR 121.2, that are intended for use in organ transplantation and labeled ''For use in organ transplantation only.''

(e) *Manufacture means,* but is not limited to, any or all steps in the recovery, processing, storage, labeling, packaging, or distribution of any human cell or tissue, and the screening or testing of the cell or tissue donor.

(f) *Minimal manipulation* means:

(1) For structural tissue, processing that does not alter the original relevant characteristics of the tissue relating to the tissue's utility for reconstruction, repair, or replacement; and

(2) For cells or nonstructural tissues, processing that does not alter the relevant biological characteristics of cells or tissues.

(g) *Transfer* means the placement of human reproductive cells or tissues into a human recipient.

(h) *Biohazard legend* appears on the label as follows and is used to mark HCT/Ps that present a known or suspected relevant communicable disease risk.



BIOHAZARD

(i) *Blood component* means a product containing a part of human blood separated by physical or mechanical means.

(j) *Colloid* means:

(1) A protein or polysaccharide solution, such as albumin, dextran, or hetastarch, that can be used to increase or maintain osmotic (oncotic) pressure in the intravascular compartment; or

(2) Blood components such as plasma and platelets.

(k) *Crystalloid* means an isotonic salt and/or glucose solution used for electrolyte replacement or to increase intravascular volume, such as saline solution, Ringer's lactate solution, or 5 percent dextrose in water.

(l) *Directed reproductive donor* means a donor of reproductive cells or tissue (including semen, oocytes, and embryos to which the donor contributed the spermatozoa or oocyte) to a specific recipient, and who knows and is known by the recipient before donation. The term directed reproductive donor does not include a sexually intimate partner under §1271.90.

(m) *Donor* means a person, living or dead, who is the source of cells or tissue for an HCT/P.

(n) *Donor medical history interview means* a documented dialog about the donor's medical history and relevant social behavior, including activities, behaviors, and descriptions considered to increase the donor's relevant communicable disease risk:

(1) With the donor, if the donor is living and able to participate in the interview, or

(2) If not, with an individual or individuals able to provide the information sought in the interview (e.g., the donor's next-of-kin, the nearest available relative, a member of the donor's household, an individual with an affinity relationship, and/or the primary treating physician).

(o) *Physical assessment of a cadaveric donor* means a limited autopsy or recent antemortem or postmortem physical examination of the donor to assess for signs of a relevant communicable disease and for signs suggestive of any risk factor for a relevant communicable disease.

(p) *Plasma dilution* means a decrease in the concentration of the donor's plasma proteins and circulating antigens or antibodies resulting from the transfusion of blood or blood components and/or infusion of fluids.

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(q) *Quarantine* means the storage or identification of an HCT/P, to prevent improper release, in a physically separate area clearly identified for such use, or through use of other procedures, such as automated designation.

(r) *Relevant communicable disease agent or disease* means:

(1)(i) For all human cells and tissues, a communicable disease or disease agent listed as follows:

(A) Human immunodeficiency virus, types 1 and 2;

(B) Hepatitis B virus;

(C) Hepatitis C virus;

(D) Human transmissible spongiform encephalopathy, including Creutzfeldt-Jakob disease; and

(E) *Treponema pallidum*.

(ii) For viable, leukocyte-rich cells and tissues, a cell-associated disease agent or disease listed as follows:

(A) Human T-lymphotropic virus, type I; and

(B) Human T-lymphotropic virus, type II.

(iii) For reproductive cells or tissues, a disease agent or disease of the genitourinary tract listed as follows:

(A) *Chlamydia trachomatis*; and

(B) *Neisseria gonorrhea*.

(2) A disease agent or disease not listed in paragraph (r)(1) of this section:

(i) For which there may be a risk of transmission by an HCT/P, either to the recipient of the HCT/P or to those people who may handle or otherwise come in contact with it, such as medical personnel, because the disease agent or disease:

(A) Is potentially transmissible by an HCT/P and

(B) Either of the following applies:

(*1*) The disease agent or disease has sufficient incidence and/or prevalence to affect the potential donor population, or

(*2*) The disease agent or disease may have been released accidentally or intentionally in a manner that could place potential donors at risk of infection;

(ii) That could be fatal or life-threatening, could result in permanent impairment of a body function or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of body function or permanent damage to a body structure; and

(iii) For which appropriate screening measures have been developed and/or an appropriate screening test for donor specimens has been licensed, approved, or cleared for such use by FDA and is available.

(s) *Relevant medical records* means a collection of documents that includes a current donor medical history interview; a current report of the physical assessment of a cadaveric donor or the physical examination of a living donor; and, if available, the following:

(1) Laboratory test results (other than results of testing for relevant communicable disease agents required under this subpart);

(2) Medical records;

(3) Coroner and autopsy reports; and

(4) Records or other information received from any source pertaining to risk factors for relevant communicable disease (e.g., social behavior, clinical signs and symptoms of relevant communicable disease, and treatments related to medical conditions suggestive of risk for relevant communicable disease).

(t) *Responsible person* means a person who is authorized to perform designated functions for which he or she is trained and qualified.

(u) *Urgent medical need* means that no comparable HCT/P is available and the recipient is likely to suffer death or serious morbidity without the HCT/P.

(v) *Act* means the Federal Food, Drug, and Cosmetic Act.

(w) *PHS Act* means the Public Health Service Act.

(x) *FDA* means the Food and Drug Administration.

(y) *Adverse reaction* means a noxious and unintended response to any HCT/P for which there is a reasonable possibility that the HCT/P caused the response.

(z) *Available for distribution* means that the HCT/P has been determined to meet all release criteria.

(aa) *Complaint* means any written, oral, or electronic communication about a distributed HCT/P that alleges:

(1) That an HCT/P has transmitted or may have transmitted a communicable disease to the recipient of the HCT/P; or

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(2) Any other problem with an HCT/P relating to the potential for transmission of communicable disease, such as the failure to comply with current good tissue practice.

(bb) *Distribution* means any conveyance or shipment (including importation and exportation) of an HCT/P that has been determined to meet all release criteria, whether or not such conveyance or shipment is entirely intrastate. If an entity does not take physical possession of an HCT/P, the entity is not considered a distributor.

(cc) *Establish and maintain* means define, document (in writing or electronically), and implement; then follow, review, and, as needed, revise on an ongoing basis.

(dd) *HCT/P deviation* means an event:

(1) That represents a deviation from applicable regulations in this part or from applicable standards or established specifications that relate to the prevention of communicable disease transmission or HCT/P contamination; or

(2) That is an unexpected or unforeseeable event that may relate to the transmission or potential transmission of a communicable disease or may lead to HCT/P contamination.

(ee) *Importer of record* means the person, establishment, or its representative responsible for making entry of imported goods in accordance with all laws affecting such importation.

(ff) *Processing* means any activity performed on an HCT/P, other than recovery, donor screening, donor testing, storage, labeling, packaging, or distribution, such as testing for microorganisms, preparation, sterilization, steps to inactivate or remove adventitious agents, preservation for storage, and removal from storage.

(gg) *Quality audit* means a documented, independent inspection and review of an establishment's activities related to core CGTP requirements. The purpose of a quality audit is to verify, by examination and evaluation of objective evidence, the degree of compliance with those aspects of the quality program under review.

(hh) *Quality program* means an organization's comprehensive system for manufacturing and tracking HCT/Ps in accordance with this part. A quality program is designed to prevent, detect, and correct deficiencies that may lead to circumstances that increase the risk of introduction, transmission, or spread of communicable diseases.

(ii) *Recovery* means obtaining from a human donor cells or tissues that are intended for use in human implantation, transplantation, infusion, or transfer.

(jj) *Storage* means holding HCT/Ps for future processing and/or distribution.

(kk) *Validation* means confirmation by examination and provision of objective evidence that particular requirements can consistently be fulfilled. Validation of a process, or *process validation*, means establishing by objective evidence that a process consistently produces a result or HCT/P meeting its predetermined specifications.

(ll) *Verification* means confirmation by examination and provision of objective evidence that specified requirements have been fulfilled.

(mm) *Importer* means a company or individual in the United States that is the owner, consignee, or recipient, at the time of entry, of the foreign establishment's HCT/P that is imported into the United States.

(nn) *United States agent* means a person residing or maintaining a place of business in the United States whom a foreign establishment designates as its agent. This definition excludes mailboxes, answering machines or services, or other places where an individual acting as the foreign establishment's agent is not physically present.

[66 FR 5466, Jan. 19, 2001, as amended at 68 FR 3826, Jan. 27, 2004; 69 FR 29829, May 25, 2004; 69 FR 68680, Nov. 24, 2004; 81 FR 60223, Aug. 31, 2016]

§ 1271.10 Are my HCT/P's regulated solely under section 361 of the PHS Act and the regulations in this part, and if so what must I do?

(a) An HCT/P is regulated solely under section 361 of the PHS Act and the regulations in this part if it meets all of the following criteria:

(1) The HCT/P is minimally manipulated;

(2) The HCT/P is intended for homologous use only, as reflected by the labeling, advertising, or other indications of the manufacturer's objective intent;

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