

HCT/P Donor Screening/Testing and Requests for Exemption

Scott A. Brubaker

Acting Director, Division of Human Tissues
Office of Cellular Therapy & Human Tissue
Office of Therapeutic Products
CBER | US FDA

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Informal Communication Disclaimer



My comments are an informal communication and represent my own best judgment. These comments do not bind or obligate FDA.

Disclosures



I have no financial interests to disclose regarding relationships with commercial organizations or companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.



Learning Objectives



- Understand that medical products of human origin have transmitted a wide variety of disease agents and diseases
- Describe requirements for HCT/P donor screening, donor testing, and making a donor eligibility determination
- Identify when a request for an exemption or alternative is indicated, how to submit, and helpful tips to consider

Note: This presentation does not include a complete list of regulatory requirements. Refer to 21 CFR part 1271 and applicable guidance documents.



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Disease Transmission by “Tissue” Allografts (1954 to 2011 ... worldwide)



HIV-1	Fresh bone, Frozen tendon
HBV	Fresh cornea, Cryopreserved heart valve
HCV	Frozen bone, Frozen tendon, Cryopreserved vein, Cryopreserved cardiac patch
CMV	Fresh skin
EBV	Fresh nerve
HTLV-1	Frozen bone
Rabies	Fresh cornea, Fresh artery (“organ” use)
Herpes simplex	Fresh cornea
CJD	Fresh cornea, Freeze-dried dura mater
Tuberculosis	Frozen bone, Cryopreserved heart valve, Freeze-dried dura mater
Yeast, Fungus	Fresh cornea, Cryopreserved heart valve
Bacteria	Fresh cornea, Fresh skin, Fresh cartilage, Frozen tendon, Frozen bone, Frozen pericardium, Cryopreserved heart valve

Disease Transmission by “MPHO*”

Disease or Disease Agent	Blood	Tissue	Organ	HSC
HIV	X	X	X	X
HBV, HCV, HTLV-I	X	X	X	X
Syphilis			X	
CMV, EBV	X	X	X	X
Bacteria	X	X	X	X
Fungi		X	X	X
CJD	variant	classic		
Parvovirus	X		X	X
Toxoplasmosis	X		X	X

*Medical Products of Human Origin

Disease Transmission by “MPHO”

Disease or Disease Agent	Blood	Tissue	Organ	HSC
Dengue Virus	X		X	X
West Nile Virus	X		X	
Rabies Virus		X	X	
Tuberculosis		X	X	
Herpes simplex		X	X	
Malaria	X		X	X
<i>Trypanosoma cruzi</i>	X		X	
Filariae (<i>W. bancrofti</i>)	X		X	
Leishmaniasis	X		X	
Babesiosis	X			

Other Disease Transmissions by “MPHO”



Blood	Hepatitis E virus, Tick-borne encephalitis (virus), Colorado tick fever, Rocky Mountain Spotted Fever (<i>Rickettsia rickettsia</i>)
Tissue	Non-tuberculous mycobacteria (refrigerated arterial graft)
Organ	Human papilloma virus (from hand transplant), Human herpes virus-8, adenovirus, lymphocytic choriomeningitis virus, <i>Balamuthia mandrillaris</i> (amoeba), strongyloidiasis, schistosomiasis
Hematopoietic Stem Cells (HSCs)	Scrub typhus (<i>Orientia tsutsugamushi</i>), Brucellosis

Disease Transmission – Assisted Reproductive Technology



Semen - Infection	HIV, HBV, Herpes simplex virus type 2, <i>Chlamydia trachomatis</i> , gonorrhea, <i>Ureaplasma urealyticum</i> , bacteremia/sepsis from intra-uterine insemination procedure
Semen – Metabolic, Genetic	Hypertrophic cardiomyopathy, severe congenital neutropenia, fragile X syndrome, autosomal dominant polycystic kidney disease, atopy, eczema, allergies
Ovum – Metabolic, Genetic	Cystic fibrosis
Embryo - Infection	HBV
Gestational Carrier – Antibody Mediated	Hemolytic disease of the newborn, neonatal alloimmune thrombocytopenia

Neoplastic Disease Transmission by “MPHO”

Fresh cornea	Papillary adenocarcinoma, glioma
Hematopoietic Stem Cells (HSCs)	Post transplant lymphoproliferative disorders, Non-Hodgkin's lymphoma, acute myelogenous leukemia, acute lymphocytic leukemia, chronic myelogenous leukemia, chronic lymphocytic leukemia
Organ	Post transplant lymphoproliferative disorders, Non-Hodgkin's lymphoma, renal cell carcinoma, choriocarcinoma, melanoma, sarcoma, astrocytoma, glioblastoma multiforme, medulloblastoma, adenocarcinomas (pancreas, colon, prostate, breast, lung), carcinomas (lung small-cell, lung bronchioloalveolar, hepatocellular, ovarian, urothelial, undifferentiated small-cell neuroendocrine), IgA myeloma, and multiple myeloma (+ probably more)

21 CFR Part 1271

Subpart C - Donor Eligibility

Selections are limited

21 CFR part 1271



Subpart A: General Provisions	Definitions; criteria for regulatory pathway determination (e.g., 361 HCT/P vs. 351 HCT/P)
Subpart B: Procedures for Registration and Listing	Requirements for establishment registration and listing products they manufacture
Subpart C: Donor Eligibility	Requirements for donor screening and testing for “relevant communicable disease agents and diseases,” and for making a donor eligibility determination
Subpart D: Current Good Tissue Practice	Handling and process controls to prevent the introduction, transmission, or spread of communicable diseases
Subpart E: Additional Requirements for Establishments Described in §1271.10	Reporting adverse reactions and HCT/P deviations; labeling
Subpart F: Inspection and Enforcement of Establishments Described in §1271.10	Inspection; import; orders of retention, recall, destruction, and cessation of manufacturing

Subparts D and E are not implemented for reproductive HCT/Ps except these in subpart D:
§ 1271.150(c) Compliance with applicable requirements and § 1271.155 Exemptions and alternatives

Definition of HCT/Ps



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.

21 CFR 1271.3(d)

Encompasses a wide variety of product types from living donors as well as from deceased donors.

A Few Examples



<https://wtop.com/health-fitness/2018/01/valuable-gift-wtop/>
Jenny Glick/WTOP

DE Final Rule - Applicability



HCT/Ps recovered on or after May 25, 2005.

- HCT/Ps described in 21 CFR 1271.10(a) regulated solely under the authority of section 361 of the Public Health Service (PHS) Act and 21 CFR part 1271 regulations
 - Pre-market review not required
- HCT/Ps regulated as drugs, devices, and/or biological products under the authority of the Federal Food, Drug & Cosmetic (FD&C) Act and/or section 351 of the PHS Act, and applicable regulations, including 21 CFR part 1271
 - Premarket review required (e.g., investigational new drug (IND) application, biological license application (BLA))

21 CFR 1271.1(b)

Regulatory Authority



Section 361 of the PHS Act

- FDA is an agency within the Department of Health and Human Services (HHS) and, by delegation from the Surgeon General and the Secretary of HHS, has authority to create and enforce regulations as it deems necessary to prevent the introduction, transmission, or spread of communicable diseases from foreign countries into the United States or from State to State (42 U.S.C. 264).
- Under this authority, FDA has promulgated regulations in Title 21 of the Code of Federal Regulations (CFR) part 1271, regarding human cells, tissues, or cellular or tissue-based products (HCT/Ps). Since HCT/Ps contain components from the human body, they pose some risk of carrying pathogens that could cause disease in health-care personnel, other handlers of tissue, recipients, and family members or other close contacts of recipients.

Definitions



21 CFR 1271.3(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.

21 CFR 1271.3(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.

21 CFR 1271.3(t)

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

Note that 21 CFR 1271.3 contains 40 definitions

Donor Eligibility



§ 1271.45 What requirements does this subpart contain?

(a) General.

This subpart sets out requirements for determining donor eligibility, including donor screening and testing. The requirements contained in this subpart are a component of current good tissue practice (CGTP) requirements. Other CGTP requirements are set out in subpart D of this part.

Donor Eligibility



§ 1271.45 What requirements does this subpart contain?

(b) Donor-eligibility determination required.

A donor-eligibility determination, based on donor screening and testing for relevant communicable disease agents and diseases, is required for all donors of cells or tissue used in HCT/Ps, except as provided under § 1271.90. In the case of an embryo...

Note that § 1271.90 includes exceptions for autologous use and for reproductive use.

Donor Eligibility



§ 1271.45 What requirements does this subpart contain?

(c) Prohibition on use.

An HCT/P must not be implanted, transplanted, infused, or transferred until the donor has been determined to be eligible, except as provided under §§ 1271.60(d), 1271.65(b), and 1271.90 of this subpart.

Note that § 1271.60(d) includes use in cases of ‘urgent medical need’ and § 1271.65(b) includes limited uses of HCT/Ps from an ineligible donor.

Subpart C - Donor Eligibility



§ 1271.47 What procedures must I establish and maintain?

- Review and approval; availability; departures from procedures; may adopt standard procedures of others

§ 1271.50 How do I determine whether a donor is eligible?

- Determination based on screening and testing; eligible donor; determination documented by a *responsible person*

§ 1271.55 What records must accompany an HCT/P after the donor-eligibility determination is complete; and what records must I retain?

- Accompanying records including a distinct ID code; summary of records; deletion of personal information; record retention requirements

Subpart C - Donor Eligibility



§ 1271.60 What quarantine and other requirements apply before the donor-eligibility determination is complete?

- Quarantine; identification; shipping; use in urgent medical need

§ 1271.65 How do I store an HCT/P from a donor determined to be ineligible, and what uses of the HCT/P are not prohibited?

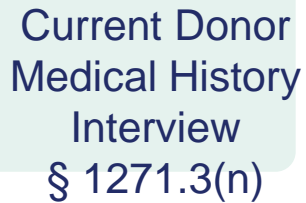
- Storage; limited uses of product from an ineligible donor

§ 1271.75 How do I screen a donor?

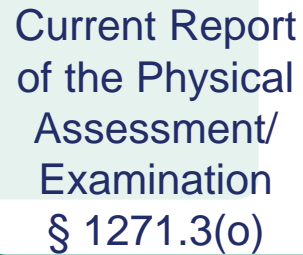
- Risk factors for, and clinical evidence of, relevant communicable disease agents and diseases (RCDADs) and communicable disease risks associated with xenotransplantation; *relevant medical records*

A box with an orange background and a rounded orange border containing the text "Relevant Medical Records" and "§ 1271.3(s)".

Relevant
Medical
Records
§ 1271.3(s)

A box with a green background and a rounded green border containing the text "Current Donor Medical History Interview" and "§ 1271.3(n)".


Current Donor
Medical History
Interview
§ 1271.3(n)

A box with a green background and a rounded green border containing the text "Current Report of the Physical Assessment/ Examination" and "§ 1271.3(o)".

Current Report
of the Physical
Assessment/
Examination
§ 1271.3(o)

A box with a dark red background and a rounded green border containing the text "Other Records (If Available)".


Other Records
(If Available)

A box with a dark red background and a rounded dark red border containing the text "Additional Lab Test Results".

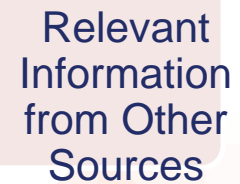
Additional
Lab Test
Results

A box with a dark red background and a rounded dark red border containing the text "Medical Records".

Medical
Records

A box with a dark red background and a rounded dark red border containing the text "Coroner & Autopsy Reports".

Coroner &
Autopsy
Reports

A box with a dark red background and a rounded dark red border containing the text "Relevant Information from Other Sources".

Relevant
Information
from Other
Sources

Subpart C - Donor Eligibility



§ 1271.80 What are the general requirements for donor testing?

- Required testing; timing of specimen collection; use of appropriate FDA-licensed, approved, or cleared donor screening tests; tests performed by a CLIA certified laboratory or CMS equivalent; ineligible donors (includes *plasma dilution*)

§ 1271.85 What donor testing is required for different types of cells and tissues?

- Viable, leukocyte-rich cells/tissue; reproductive cells/tissues; retesting anonymous semen donors

§ 1271.90 Are there other exceptions and what labeling requirements apply?

- DE not required; exceptions for autologous use and reproductive use; required labeling

Timing of Specimen Collection



- Donor specimen(s) to be used for donor testing **must** be collected at the time of recovery, or **up to 7 days before or after recovery** of HCT/Ps
- For donors of peripheral blood stem/progenitor cells, bone marrow (if not excepted under §1271.3(d)(4)), or oocytes:
 - The specimen for testing may be collected **up to 30 days before** recovery (the “7 days after” recovery still applies)

Note: Because these donor types, or recipients of their HCT/Ps, may undergo conditioning regimens beginning more than 7 days before recovery, 21 CFR [1271.80\(b\)](#) permits collecting the donor specimen for testing up to 30 days before recovery. This does NOT extend to semen donors, to donors of peripheral blood mononuclear cells (PBMCs), or to cord blood donors.

Plasma Dilution



Refer to definitions for: plasma dilution (§ 1271.3(p)); blood component (§ 1271.3(i)); colloid (§ 1271.3(j)); and crystalloid (§ 1271.3(k))

A donor is ineligible if plasma dilution is sufficient to affect the results of communicable disease testing, unless

- a pre-transfusion/infusion specimen is used and tests negative, or
- an appropriate algorithm is applied to show plasma dilution is not sufficient to affect test results

Refer to the 2007 HCT/P DE guidance for discussion of circumstances when an algorithm should be used and for an example algorithm.

21 CFR 1271.80(d)(2)

Testing Laboratory Certification



Required testing under § 1271.80 must be performed by a laboratory that either is certified to perform such testing on human specimens under the Clinical Laboratory Improvement Amendments of 1988 (42 U.S.C. 263a) and 42 CFR part 493, or has met equivalent requirements as determined by the Centers for Medicare and Medicaid Services.



21 CFR 1271.80(c)

Relevant Communicable Disease Agents and Diseases



- Those specifically listed in the regulations (§1271.3(r)(1)); and
- Those that meet definitional elements/factors of an RCDAD (§1271.3(r)(2)).
 - Notified through publication of a guidance document
 - Factors consider ...
 - risk of transmission [by an HCT/P, includes known transmissions and the potential for transmission];
 - severity of effect [significant health risk; morbidity/mortality]; and
 - availability of appropriate [donor] screening measures and tests.

Relevant Communicable Disease Agents and Diseases



For all HCT/Ps:

- Human immunodeficiency virus, types 1 and 2 (HIV-1/2)
- Hepatitis B virus (HBV)
- Hepatitis C virus (HCV)
- Human transmissible spongiform encephalopathy (hTSE), including Creutzfeldt-Jakob disease (CJD) and variant CJD (vCJD)
- *Treponema pallidum* (agent that causes syphilis)
- Vaccinia**
- Sepsis**
- West Nile Virus (WNV)**
- Zika virus (ZIKV)**

** Not considered RCDADs at the time of publication of the Tissue Regulations in 2004. They were added to the list of RCDADs through publication of the 2007 DE Guidance (vaccinia, sepsis, WNV) and 2016 Zika Guidance (ZIKV).

For viable, leukocyte-rich cells and tissues:

- Human T-lymphotropic virus, type I and type II (HTLV-I/II)

For reproductive cells and tissues:

- *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG)

Donor Screening and Testing



Agent	Required for	Screening	Testing*
HIV 1/2	All HCT/Ps	X	X
HBV	All HCT/Ps	X	X
HCV	All HCT/Ps	X	X
<i>Treponema pallidum</i>	All HCT/Ps	X	X
TSE	All HCT/Ps	X	
WNV	HCT/Ps	X	X (living donors only)
Sepsis	All HCT/Ps	X	
Vaccinia	All HCT/Ps	X	
ZIKV	All HCT/Ps	X	
HTLV I/II	Viable, leukocyte-rich HCT/Ps	X	X
CMV (not an RCDAD)	Viable, leukocyte-rich HCT/Ps		X
<i>Chlamydia trachomatis</i>	Reproductive HCT/Ps	X	X
<i>Neisseria gonorrhoeae</i>	Reproductive HCT/Ps	X	X

* More than one test may be necessary to adequately and appropriately test for a single agent (i.e., serology and NAT). 32

Adequate and Appropriate Tests



HIV-1 FDA-licensed donor screening test: <ul style="list-style-type: none"> • Anti-HIV-1 or combo test for anti-HIV-1 and anti-HIV-2, AND • NAT test for HIV-1 or combination NAT test 	HIV-2 FDA-licensed donor screening test: <ul style="list-style-type: none"> • Anti-HIV-2 or combo test for anti-HIV-1 and anti-HIV-2 	HBV FDA-licensed donor screening test: <ul style="list-style-type: none"> • Hepatitis B surface antigen (HBsAg), • Total antibody to Hepatitis B core antigen (IgG & IgM; anti-HBc), AND • NAT test for HBV 	HCV FDA-licensed donor screening test: <ul style="list-style-type: none"> • Anti-HCV, AND • NAT test for HCV or combination test
<i>Treponema pallidum</i> FDA-cleared donor screening test: <ul style="list-style-type: none"> • Nontreponemal or treponemal 	WNV FDA-licensed donor screening test: <ul style="list-style-type: none"> • NAT test for WNV 	HTLV-I/II FDA-licensed donor screening test: <ul style="list-style-type: none"> • Anti-HTLV-I/II 	CMV FDA-cleared donor screening test: <ul style="list-style-type: none"> • Anti-CMV, total IgG and IgM
<i>Chlamydia trachomatis</i> FDA-cleared diagnostic test: <ul style="list-style-type: none"> • NAT test for CT in an asymptomatic, low-prevalence population 	<i>Neisseria gonorrhoeae</i> FDA-cleared diagnostic test: <ul style="list-style-type: none"> • NAT test for NG in an asymptomatic, low-prevalence population 	<ul style="list-style-type: none"> • 2007 DE Guidance, VI.A-B. • 2015 Syphilis Tests Guidance • 2016 WNV NAT Guidance • 2016 HBV NAT Guidance 	

DE Related Guidance



- [Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products](#) (August 2007)
- [Use of Donor Screening Tests to Test Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products for Infection with *Treponema pallidum* \(Syphilis\); Guidance for Industry](#) (September 2015)
- [Use of Nucleic Acid Tests to Reduce the Risk of Transmission of Hepatitis B Virus from Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products; Guidance for Industry](#) (August 2016)
- [Use of Nucleic Acid Tests to Reduce the Risk of Transmission of West Nile Virus from Living Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products \(HCT/Ps\); Guidance for Industry](#) (September 2016, corrected May 2017)
- [Revised Recommendations for Determining Eligibility of Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products Who Have Received Human-Derived Clotting Factor Concentrates; Guidance for Industry](#) (November 2016)
- [Donor Screening Recommendations to Reduce the Risk of Transmission of Zika Virus by Human Cells, Tissues, and Cellular and Tissue-Based Products; Guidance for Industry](#) (March 2016, updated May 2018)

FDA-licensed, approved, or cleared tests



“Testing HCT/P Donors for Relevant Communicable Disease Agents and Diseases”

<https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/testing-human-cells-tissues-and-cellular-and-tissue-based-product-hctp-donors-relevant-communicable>

“Complete List of Donor Screening Assays for Infectious Agents and HIV Diagnostic Assays”

<https://www.fda.gov/vaccines-blood-biologics/complete-list-donor-screening-assays-infectious-agents-and-hiv-diagnostic-assays>

Knowledge Check

Knowledge Check 1



Which of the following disease agents is not an RCDAD?

1. HTLV-I/II
2. Cytomegalovirus
3. Transmissible spongiform encephalopathy



21 CFR 1271.155 Exemptions and Alternatives

What if requirements are not met?

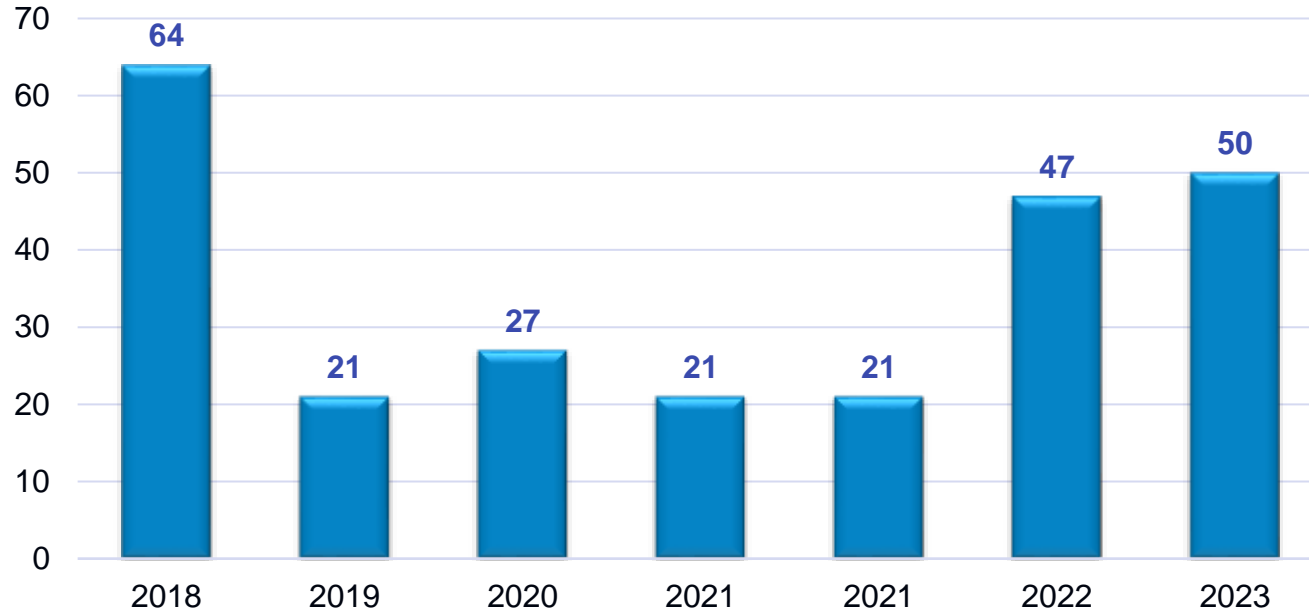
- Establishments may request an exemption from or alternative to any requirement in part 1271 subpart C (Donor Eligibility) or subpart D (Current Good Tissue Practice)
- Requests must be submitted to the OTP Office Director and include
 - Information justifying the requested exemption from the requirement,
 - or
 - A description of a proposed alternative method of meeting the requirement
- Must not begin operating under the terms of a requested exemption or alternative until the exemption or alternative has been granted

What if requirements are not met?



- FDA would consider granting an exemption or alternative requested under § 1271.155, if such action is consistent with the goals of protecting the public health and the information submitted justifies an exemption or alternative.
- Refer to Exemptions and Alternatives webpage <https://www.fda.gov/vaccines-blood-biologics/tissue-tissue-products/exemptions-and-alternatives>

DHT Activity Metric: Exemption Requests



21 CFR 1271.155 Exemptions and alternatives.

Potential Noncompliance to ...

- Required Donor Screening
 - Donor medical history interview
- Required Donor Testing
 - Specific tests
 - CLIA certified laboratory(ies), or CMS equivalent, that performed communicable disease testing of the donor
- Donor Eligibility Determination
- Pooling

Example: Human cells/tissues originally recovered for research become a component of a product intended for clinical use in human recipients ...

CGTP Requirements



- 21 CFR part 1271, subpart D
- Includes, but is not limited to:
 - Description of core CGTP requirements
 - Requirements that directly relate to preventing the introduction, transmission, or spread of communicable disease by HCT/Ps
 - Applicability of current good manufacturing practice (CGMP) requirements for drugs, and device quality system (QS) regulation requirements

Guidance for Industry

Current Good Tissue Practice (CGTP) and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)

Additional copies of this guidance are available from the Office of Communication, Outreach and Development (OCOD), (HFM-40), 1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448, or by calling 1-800-835-4709 or 301-827-1800, or e-mail ocod@fda.hhs.gov, or from the Internet at <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>

For questions on the content of this guidance, contact OCOD at the phone numbers or e-mail address listed above.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
December 2011

Excerpt from CGTP Guidance



III. CGTP REQUIREMENTS (§ 1271.150)

E. Do I Have to Follow CGTP Requirements if My HCT/Ps Are Also Regulated as a Biological Product, Drug, or Device?

Yes, CGTP requirements as well as drug current good manufacturing practice (CGMP) requirements or device quality system (QS) regulation requirements apply.

The current CGMP regulations in 21 CFR parts 210 and 211 or the QS regulation in 21 CFR part 820 apply to an HCT/P depending upon whether the product is regulated as a drug, device or biological product (§ 1271.150(d)) (see especially, §§ 210.1(c), 210.2, 211.1, and 820.1).

These CGMP and QS regulations supplement the CGTP requirements, and in the event that a regulation in part 1271 is in conflict with a requirement in parts 210, 211, or 820, the regulations more specifically applicable to the product in question will supersede the more general.

CGTP vs. CGMP vs. QS



- CGTP requirements not completely covered by corresponding CGMP requirements or QS regulations
 - All donor eligibility requirements (part 1271 subpart C - Donor Eligibility);
 - Prevention of the introduction, transmission, or spread of communicable diseases (§ 1271.145);
 - Certain parts of manufacturing arrangements under a contract, agreement, or other arrangement (§ 1271.150(c)(1)(ii) and (iii));
 - Procedures for sharing with other establishments information pertaining to possible contamination or potential for transmission of communicable disease (§ 1271.160(b)(2));

CGTP vs. CGMP vs. QS



- CGTP requirements not completely covered by corresponding CGMP requirements or QS regulations
 - Audits (§ 1271.160(c)); (CGMPs only)
 - Prohibition on pooling (§ 1271.220(b));
 - Predistribution shipment (§ 1271.265(b))
 - HCT/P availability for distribution only after donor eligibility established (§ 1271.265(c)(2));
 - Packaging and shipping requirements (§ 1271.265(d));

CGTP vs. CGMP vs. QS



- CGTP requirements not completely covered by corresponding CGMP requirements or QS regulations
 - Recordkeeping for 10 years (§ 1271.270(d)) (but facility cleaning and sanitation records for 3 years (§ 1271.190(d)(2)); and
 - Tracking (§ 1271.290(a) through (g))



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Helpful Tips for Submitting a Request



- Letter summarizing the information and relevant regulatory deficiencies
- For reproductive HCT/Ps: relationship of gamete donor to recipient (anonymous, directed, sexually intimate partner)
- Date of recovery of HCT/Ps
- Donor medical history interview questionnaire documentation
- Physical examination/assessment record
- Donor test results provided by the testing lab
- Date and documentation of the DE determination
- CLIA-certification of the laboratory(ies)
- Tradename of each test and manufacturer of each test performed
- FDA Establishment Identifier (FEI) number (when applicable)

Helpful Tips for Submitting a Request



For HCT/Ps regulated as drugs, devices and/or biological products, we encourage sponsors to:

- Discuss the request during early communications with the FDA (e.g., INTERACT, Pre-IND meeting)
- Submit the request prior to submitting the IND/IDE application to ensure adequate time for FDA review
- Avoid placement of your IND/IDE on clinical hold

Helpful Tips for Submitting a Request



For HCT/Ps regulated as drugs, devices and/or biological products, we encourage sponsors to include supporting documentation and relevant valid scientific data regarding how risk of communicable disease transmission is mitigated:

- Description of the manufacturing process of your product
- Description of donor eligibility determination, donor screening and donor testing
- In-process and final product testing performed during your manufacturing process to mitigate the risk of communicable disease transmission

DHT Activity Metric: Product Reviews



	2018	2019	2020	2021	2022	2023
IND	55	34	88	65	70	52
BLA	19	16	<5	<5	14	17
510(K)	<5	0	<5	<5	<5	<5
Pre-Sub	-	-	-	<5	15	<10
Non-CBER Consult	-	-	-	-	-	<10

Pre-INDs, original submissions, amendments, supplements,
and inter-center consults (i.e., HCT/P donor eligibility,
applicable CGTPs, donor screening tests)

Review deadlines are generally guided by MDUFA & PDUFA
(Medical Device User Fee Amendments, Prescription Drug User Fee Act)

Knowledge Check

Knowledge Check 2



An HCT/P donor eligibility determination is based on the results of:

1. Donor screening only
2. Donor testing only
3. Donor screening and donor testing

“That men do not learn very much from the lessons of history is the most important of all the lessons of history.”

Aldous Huxley (1894-1963)



<http://www.directionjournal.com/vision/gauld.html>

Looking Ahead



What DE process will you
investigate ...
how can it be improved?

Resources



21 CFR part 1271

<https://www.ecfr.gov/cgi-bin/text-idx?SID=f6f44f140b31543c17e0a8974f1500fd&mc=true&node=pt21.8.1271&rgn=div5>

The screenshot displays the eCFR (Electronic Code of Federal Regulations) website. At the top, there is a navigation bar with links for 'Browse', 'Search', 'Recent Changes', 'Corrections', 'Reader Aids', and 'My eCFR'. Below this, the 'Code of Federal Regulations' logo is prominently displayed, along with the text 'A point in time eCFR system'. The main content area is titled 'Title 21' and shows 'Part 1271'. A sidebar on the left contains links for 'Table of Contents', 'Timeline', 'Go to Date', 'Compare Dates', 'Search', 'Subscribe', and 'Share'. The main text area displays 'PART 1271 - HUMAN CELLS, TISSUES, AND CELLULAR AND TISSUE-BASED PRODUCTS' with its authority and source. Below this, it shows 'Subpart A - General Provisions' and the beginning of § 1271.1, which discusses the purpose and scope of the part.

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Title 21

Displaying title 21, up to date as of 3/01/2022. Title 21 was last amended 3/01/2022. [view historical versions](#)

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PART 1271 - HUMAN CELLS, TISSUES, AND CELLULAR AND TISSUE-BASED PRODUCTS

Authority: 42 U.S.C. 216, 243, 263a, 264, 271.

Source: 56 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(c), and 820.1(a) of this chapter, is to create an electronic registration and listing system for

Resources



Tissue and Tissue Products (homepage)

<https://www.fda.gov/BiologicsBloodVaccines/TissueTissueProducts/default.htm>

Tissue Guidances

<https://www.fda.gov/vaccines-blood-biologics/biologics-guidances/tissue-guidances>

Safety & Availability (Biologics)

<https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics>

Resources



Subscribe for CBER Updates

<https://www.fda.gov/vaccines-blood-biologics/news-events-biologics#subscribe>



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Options for Obtaining a Regulatory Classification



Obtain a Recommendation

Tissue Reference Group (TRG)

<https://www.fda.gov/vaccines-blood-biologics/tissue-tissue-products/tissue-reference-group>
SOPP 8004 <https://www.fda.gov/media/85648/download>

Pre-RFD

Guidance for Industry: How to Prepare a Pre-Request for Designation

<https://www.fda.gov/media/102706/download>

Obtain a Decision

Request for Designation (RFD)

<https://www.fda.gov/CombinationProducts/RFDProcess/default.htm>

Summary



- Use of HCT/Ps has led to risks to public health due to transmissions of a variety of disease agents and diseases.
- Donor eligibility requirements are applicable to all HCT/Ps regardless of how the product is regulated.
- Donor screening and donor testing for RCDADs, and screening for risks associated with xenotransplantation, are required for making a donor eligibility determination.
- You may consider submitting to FDA a request for an exemption or alternative if any donor eligibility or CGTP requirements are not met.

OTP Contact Information



Scott A. Brubaker

scott.brubaker@fda.hhs.gov



“351 HCT/P” Regulatory Questions

Contact the Regulatory Management Staff at:

OTPRPMS@fda.hhs.gov

240-402-8190

“361 HCT/P” Regulatory Questions

Contact OCOD (refer to Lorrie’s presentation)

OTP Learn Webinar Series <https://www.fda.gov/vaccines-blood-biologics/news-events-biologics/otp-learn>

CBER website

<http://www.fda.gov/BiologicsBloodVaccines>



Thank you for your kind attention!