HCT/P Establishment Registration and Product Listing

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Center for Biologics Evaluation and Research

FDA Workshop for Reproductive Tissue Industry
October 1, 2020

Outline

- HCT/P Establishment Registration and Listing
  - Final Rule
  - Exceptions
  - 21 CFR part 1271, subpart B
- Electronic Registration System
  - Updated Version of eHCTERS (Released November 2018)
  - Registration Summary Report
  - Public Query Application
- Frequently asked questions

HCT/P Establishment Registration & Listing

Final Rule and Exceptions

Final Rule – August 31, 2016*

- Title: “Requirements for Foreign and Domestic Establishment Registration and Listing for Human Drugs, Including Drugs That Are Regulated Under a Biologics License Application, and Animal Drugs”
- Amends regulations governing drug establishment registration and listing, including certain regulations in 21 CFR part 1271
- Effective date: November 29, 2016
- Compliance date: November 29, 2017

* 81 Federal Register 60170

August 2016 Final Rule – Summary of Changes in 21 CFR 1271

- Registration and listing requirements in subpart B of part 1271 apply to HCT/Ps that meet the criteria in § 1271.10(a) – regulated solely under section 361 of the Public Health Service (PHS) Act, *"361 HCT/Ps".*
- HCT/Ps regulated as drugs, devices, and/or biological products under section 351 of the PHS Act and/or the Federal Food, Drug, and Cosmetic Act are subject to registration and listing under part 207 or part 807 rather than part 1271.

Note: This means establishments that manufacture biological products or HCT/Ps that are regulated as medical devices no longer register in the tissue establishment registration system.

§ 1271.1

August 2016 Final Rule – Summary of Changes in 21 CFR 1271 (Continued)

- Requires electronic submission of registration information, unless waived* in certain circumstances
- Amended the timeframe for reporting certain changes (e.g. ownership & location)
- Requires foreign establishments to provide ***importer*** information

* Note: Waiver requests must be submitted in writing to CBER (§ 1271.23)

Establishment Registration & Listing

- **Establishments** that **manufacture** 361 HCT/Ps must register and list their HCT/Ps

  - Provide information about the establishment and the products that they manufacture
  - Applies to domestic and foreign establishments

§ 1271.10(b)

Definitions

- **Establishment**
  - A place of business under one management, at **one general physical location**, that engages in the manufacture of HCT/Ps. Includes:
    - Individual, partnership, corporation, association, or other legal entity
    - Facilities that engage in contract manufacturing services
- **Manufacture**
  - 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.

§ 1271.3(b) and § 1271.3(e)

Exceptions - § 1271.15

a. Establishments that use HCT/Ps for nonclinical scientific or educational purposes

b. Establishments that remove **autologous HCT/Ps** and implant **such HCT/Ps** during the **same surgical procedure**

c. Carriers (e.g. FedEx, UPS)

d. Establishments that **only receive or store** HCT/Ps **solely for use within their own facility**, provided that no other manufacturing step is performed

e. Establishments that **only recover reproductive cells or tissue** for **immediate transfer** into the **sexually intimate partner (SIP)**

f. Individuals who **solely recover** HCT/Ps under contract, agreement or other arrangement with a registered facility (other requirements in part 1271 subparts C & D may apply)

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HCT/P Establishment Registration & Listing (361 HCT/Ps)

21 CFR Part 1271, Subpart B

Initial Registration & Listing

- Must register & list HCT/Ps within 5 days after beginning operations
- Required information:
  - Establishment legal name
  - Each physical location (address, phone #, zip code)
  - Reporting Official (name, address, phone #, email, title, signature & date)
  - HCT/P types and proprietary names (if applicable)

§ 1271.21(a) and § 1271.25

Initial Registration & Listing (Continued)

- Required information (cont.):
  - Donor Types (if applicable)
    - For reproductive cells and tissues: Sexually Intimate Partner (SIP), Directed, Anonymous
  - Manufacturing functions
    - Recover
    - Screen
    - Donor Testing
    - Process (includes testing for microorganisms)
    - Store
    - Label
    - Package
    - Distribute
  - If applicable:
    - Satellite Recovery Establishment (include FEI# for the parent manufacturing establishment)
    - Testing for Microorganisms Only

§ 1271.25(b)

Initial Registration & Listing (Continued)

- Required information (cont.):
  - Foreign establishments sending HCT/Ps to the U.S. must:
    - Register and list their HCT/Ps
    - Have a U.S. Agent who resides or maintains a place of business in the U.S. (may have more than one U.S. Agent)
    - Provide name, address, phone number, email address of the U.S. Agent(s)
  - Foreign establishment is not required to notify their U.S. Agent when shipping products.
  - FDA/CBER communicates with the U.S. Agent concerning products and scheduling of inspections.

§ 1271.25(a)(6) and § 1271.3(nn)

Initial Registration & Listing (Continued)

- Required information (cont.):
  - Each foreign establishment must submit the name, address, phone #, and email address of each **importer** that is **known to the establishment**, and the name of each person who imports or offers for import such HCT/P to the United States for purposes of importation.
    - ***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.

§ 1271.25(a)(5) and § 1271.3(mm)

§ 1271.27(b)

- FDA acceptance of an establishment registration and HCT/P listing form does not constitute determination that an establishment is in compliance with applicable rules and regulations or that the HCT/P is licensed or approved by FDA.

Changes in Registration Information

- Must submit an amendment to registration:
  - Ownership or location change, or change in the U.S. Agent information **within 30 calendar days** of the change; and
  - Other material changes at the time of change, or each June or December, whichever month occurs first after the change

§ 1271.26 and § 1271.21

Annual Update

- Required even if there are no changes
- Annual update period: Nov 15 -Dec 31
- Update HCT/P listing
- Other material changes
- Updates must include:
  - A list of each HCT/P you have begun manufacturing that had not been listed previously
  - A list of each HCT/P listed previously that you have **discontinued** manufacturing, including date of discontinuance
  - A list of each HCT/P you had discontinued previously, but have **resumed** manufacturing, including date of resumption

§ 1271.21 and § 1271.25(c)

Registration Inactivation

- If an establishment has gone out of business or is no longer manufacturing 361 HCT/Ps:
  - Establishment can inactivate their registration; or
  - CBER will inactivate registration if confirmation is received from the Office of Regulatory Affairs (ORA).

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Electronic Registration System

eHCTERS – Updated Version
Release Date: November 9, 2018

Electronic Human Cell and Tissue Establishment Registration System (eHCTERS)

- Must be used for initial registration, submitting changes and annual update, and inactivating registration
- Online instructions and link to help e-mail
- One account can manage multiple registrations

Note: CBER/OTAT stopped accepting paper registrations (Form FDA 3356) on November 29, 2017

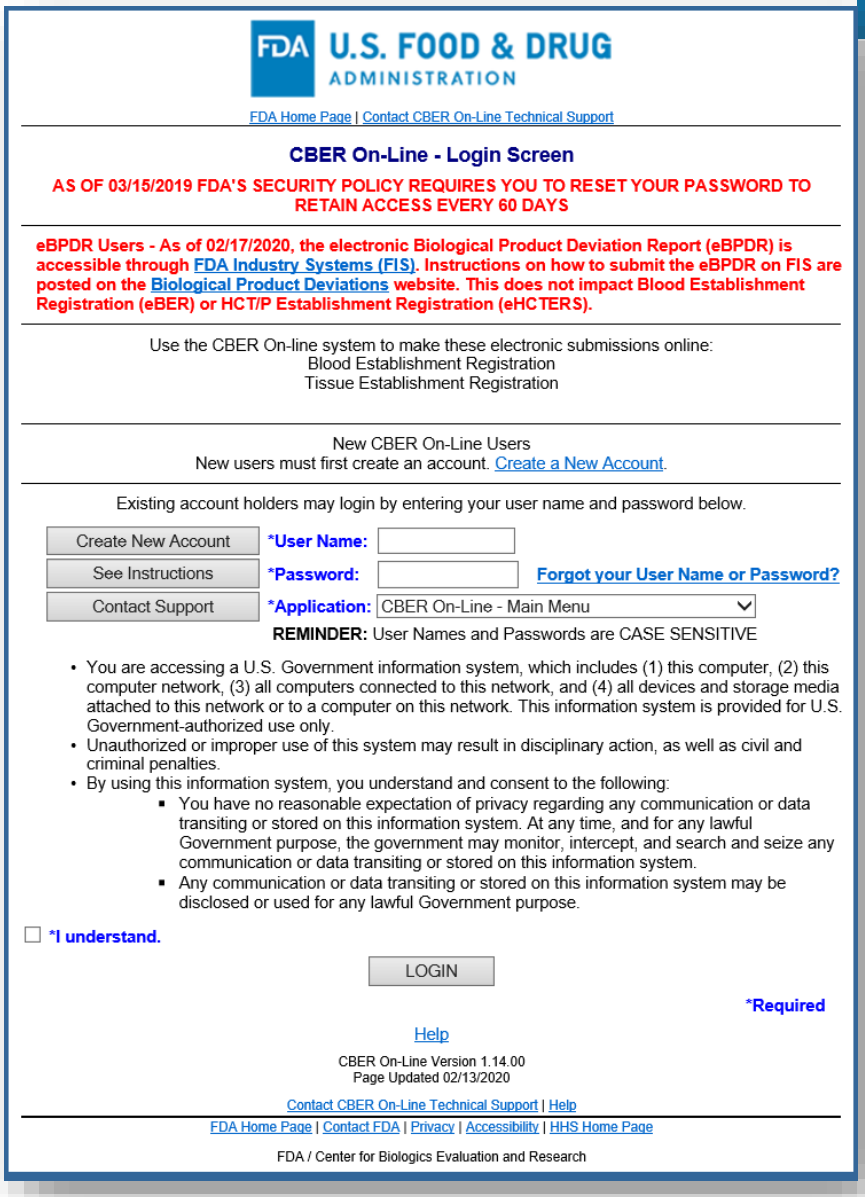
eHCTERS

CBER On-Line Login Screen

- **Create a New Account**
- **Log in with User Name & Password**

*** Security update on March 15, 2019:**

- **Enforce limit of 5 invalid login attempts within 15 minutes**
- **Enforce password reset after 60 days**



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FDA Home Page | Contact CBER On-Line Technical Support

CBER On-Line - Login Screen

AS OF 03/15/2019 FDA'S SECURITY POLICY REQUIRES YOU TO RESET YOUR PASSWORD TO RETAIN ACCESS EVERY 60 DAYS

eBPDR Users - As of 02/17/2020, the electronic Biological Product Deviation Report (eBPDR) is accessible through FDA Industry Systems (FIS). Instructions on how to submit the eBPDR on FIS are posted on the Biological Product Deviations website. This does not impact Blood Establishment Registration (eBER) or HCT/P Establishment Registration (eHCTERS).

Use the CBER On-line system to make these electronic submissions online:
Blood Establishment Registration
Tissue Establishment Registration

New CBER On-Line Users
New users must first create an account. Create a New Account.

Existing account holders may login by entering your user name and password below.

Create New Account | *User Name:
See Instructions | *Password: | Forgot your User Name or Password?
Contact Support | *Application: CBER On-Line - Main Menu

REMINDER: User Names and Passwords are CASE SENSITIVE

- You are accessing a U.S. Government information system, which includes (1) this computer, (2) this computer network, (3) all computers connected to this network, and (4) all devices and storage media attached to this network or to a computer on this network. This information system is provided for U.S. Government-authorized use only.
- Unauthorized or improper use of this system may result in disciplinary action, as well as civil and criminal penalties.
- By using this information system, you understand and consent to the following:
  - You have no reasonable expectation of privacy regarding any communication or data transiting or stored on this information system. At any time, and for any lawful Government purpose, the government may monitor, intercept, and search and seize any communication or data transiting or stored on this information system.
  - Any communication or data transiting or stored on this information system may be disclosed or used for any lawful Government purpose.

☐ *I understand.

LOGIN

*Required

Help

CBER On-Line Version 1.14.00
Page Updated 02/13/2020

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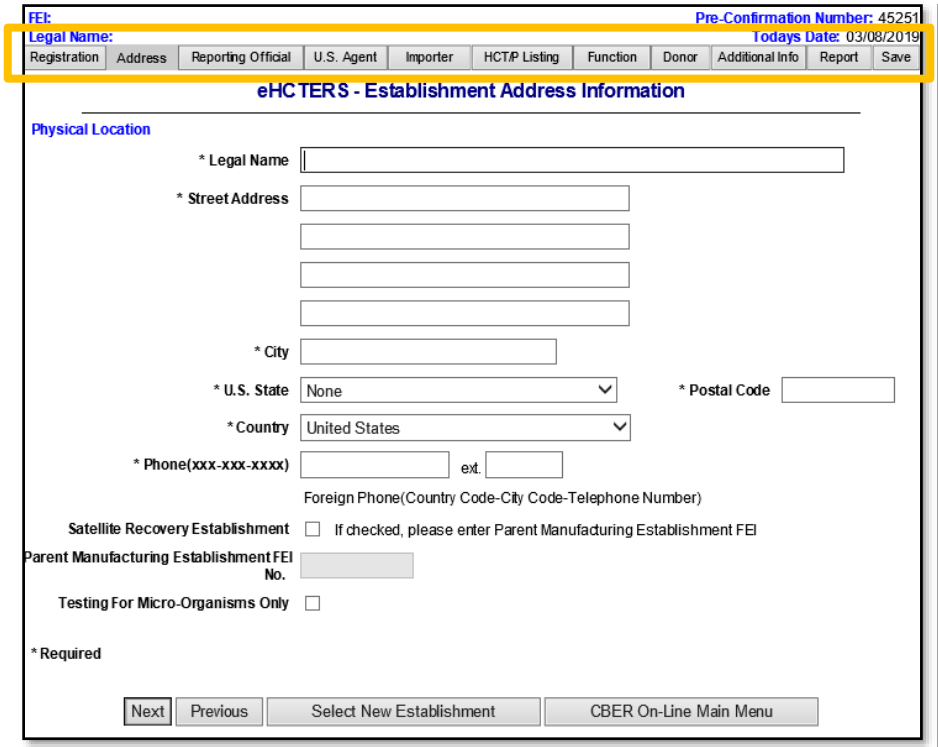
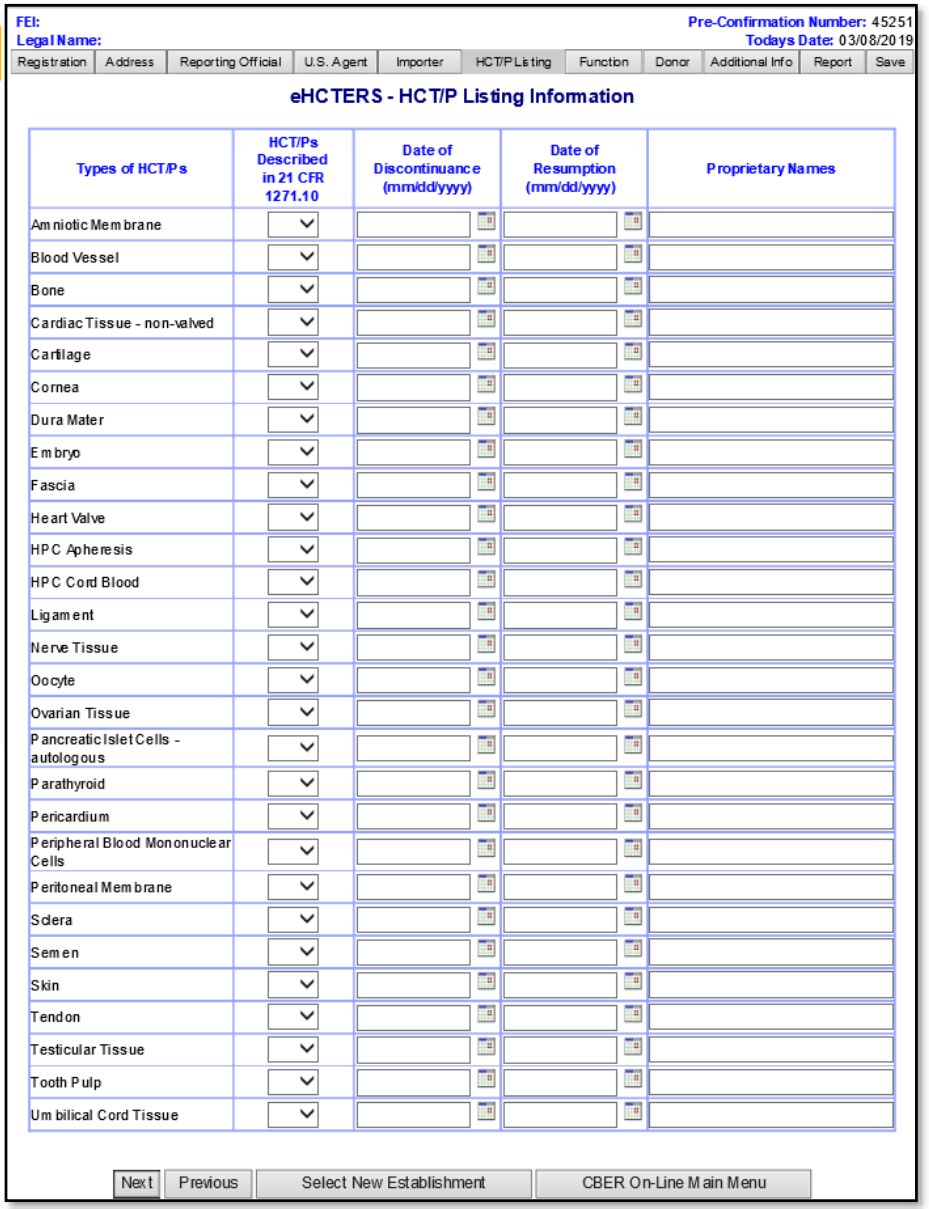
FDA / Center for Biologics Evaluation and Research

https://www.accessdata.fda.gov/sc3bf68105249a55d0-A85D0D0F-1372-5AE1-674338933A9DF71Dripts/cber/CFApps/Login/Index.cfm?CFID=14371273&CFTOKEN=

eHCTERs – Webpage Examples





- ✓ All available HCT/P types are listed on the “HCT/P Listing Information” webpage.

Process of Initial Registration

- After successful submission of initial registration:
  - The registration status is listed as “pre-registered” in eHCTERS;
  - FDA considers an establishment to be registered as soon as registration information is received.
- After FDA processes the establishment initial registration:
  - An FDA Establishment Identifier Number (FEI #) is assigned;
  - The FEI # is added to the Registration Summary Report and sent to the establishment’s Reporting Official;
  - The establishment’s registration status is changed to “Registered” in eHCTERS.

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Electronic Registration System

Registration Summary Report (Replaced Form FDA 3356)

Registration Summary Report

- Form FDA 3356 has been replaced by a Registration Summary Report of establishment registration and HCT/P listing information
  - Previous listings for HCT/Ps regulated as drugs, devices, and/or biological products have been removed from eHCTERS; they do not appear on the report.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

ESTABLISHMENT REGISTRATION AND LISTING FOR HUMAN CELLS, TISSUES, AND CELLULAR AND TISSUE-BASED PRODUCTS DESCRIBED IN 21 CFR 1271.10

FEI: [redacted]

Other FDA Registrations:
Blood:
Devices:
Drugs:

Reason For Last Submission: Annual Registration/Listing
Last Annual Registration Year: 2019
Last Registration Receipt Date: [redacted]
Summary Report Print Date: 03/06/2020

Legal Name and Location:
[redacted]
Ext.:

Reporting Official:
[redacted]

Satellite Recovery Establishment: No
Parent Manufacturing Establishment FEI No.:
Testing For Micro-Organisms Only: No

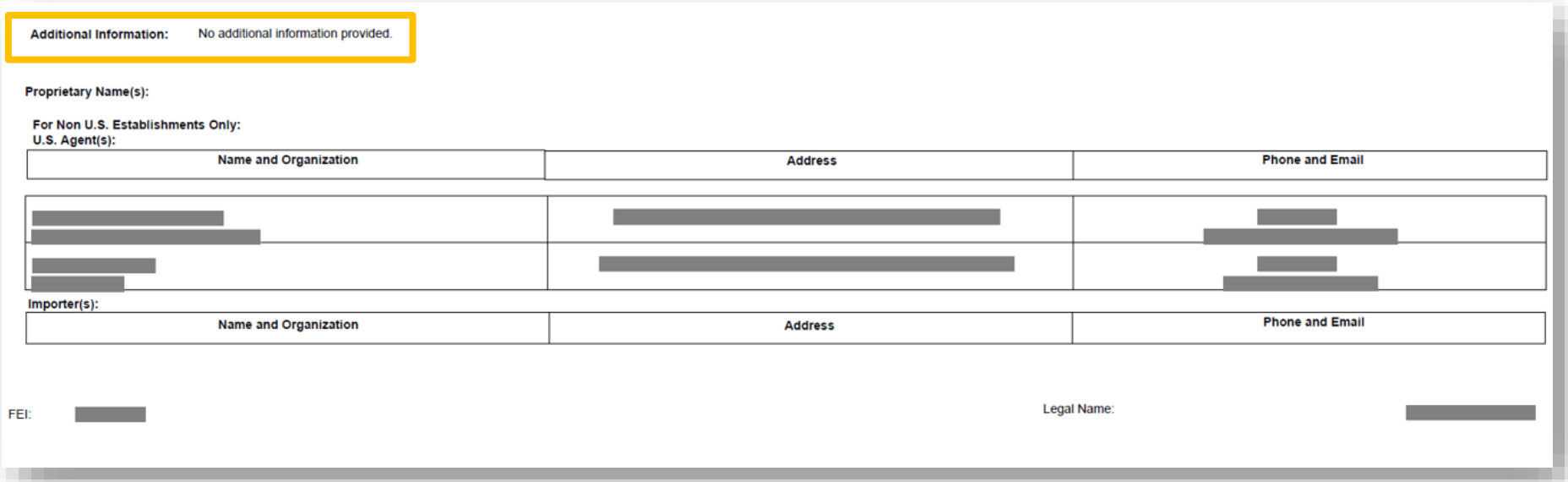
Note: FDA acceptance of an establishment registration and HCT/P listing does not constitute a determination that an establishment is in compliance with applicable rules and regulations or that the HCT/P is licensed or approved by FDA (21 CFR 1271.27(b)).

HCT/P(s)	Donor Type(s)	Establishment Functions										
		Recover	Screen	Donor Testing	Package	Process	Sto					
Amniotic Membrane												
Blood Vessel												
Bone												
Cardiac Tissue - non-valved												
Cartilage												
Cornea												
Dura Mater												
Embryo	Anonymous, Directed, SIP	X	X	X	X	X	X					
Fascia												
Heart Valve												
HPC Apheresis												
HPC Cord Blood												
Ligament												
Nerve Tissue												
Oocyte	Anonymous, Directed, SIP	X	X	X	X	X	X					
Ovarian Tissue												
Pancreatic Islet Cells - autologous												
Parathyroid												
Pericardium												
Peripheral Blood Mononuclear Cells												
Peritoneal Membrane												
Sclera												
Semen	Anonymous, Directed, SIP	X	X	X	X	X	X	X	X			
Skin												
Tendon												
Testicular Tissue												
Tooth Pulp												
Umbilical Cord Tissue												

Reason For Last Submission: Annual Registration/Listing
Last Annual Registration Year: 2019
Last Registration Receipt Date: [redacted]
Summary Report Print Date: 03/06/2020

Satellite Recovery Establishment: No
Parent Manufacturing Establishment FEI No.:
Testing For Micro-Organisms Only: No

Note: FDA acceptance of an establishment registration and HCT/P listing does not constitute a determination that an establishment is in compliance with applicable rules and regulations or that the HCT/P is licensed or approved by FDA (21 CFR 1271.27(b)).



Additional Information: No additional information provided.

Proprietary Name(s):

For Non U.S. Establishments Only:
U.S. Agent(s):

Name and Organization	Address	Phone and Email
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Importer(s):

Name and Organization	Address	Phone and Email

FEI: [redacted]

Legal Name: [redacted]

Note: For reporting ownership change, you may:

- Use “Additional Information” field in eHCTERS, or
- Email to CBER Tissue Registration at tissuereg@fda.hhs.gov, or
- Mail to “Food and Drug Administration, Center for Biologics Evaluation and Research, Document Control Center, 10903 New Hampshire Ave., Bldg. 71, Rm. G112, Silver Spring, MD 20993-0002.”

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Electronic Registration System

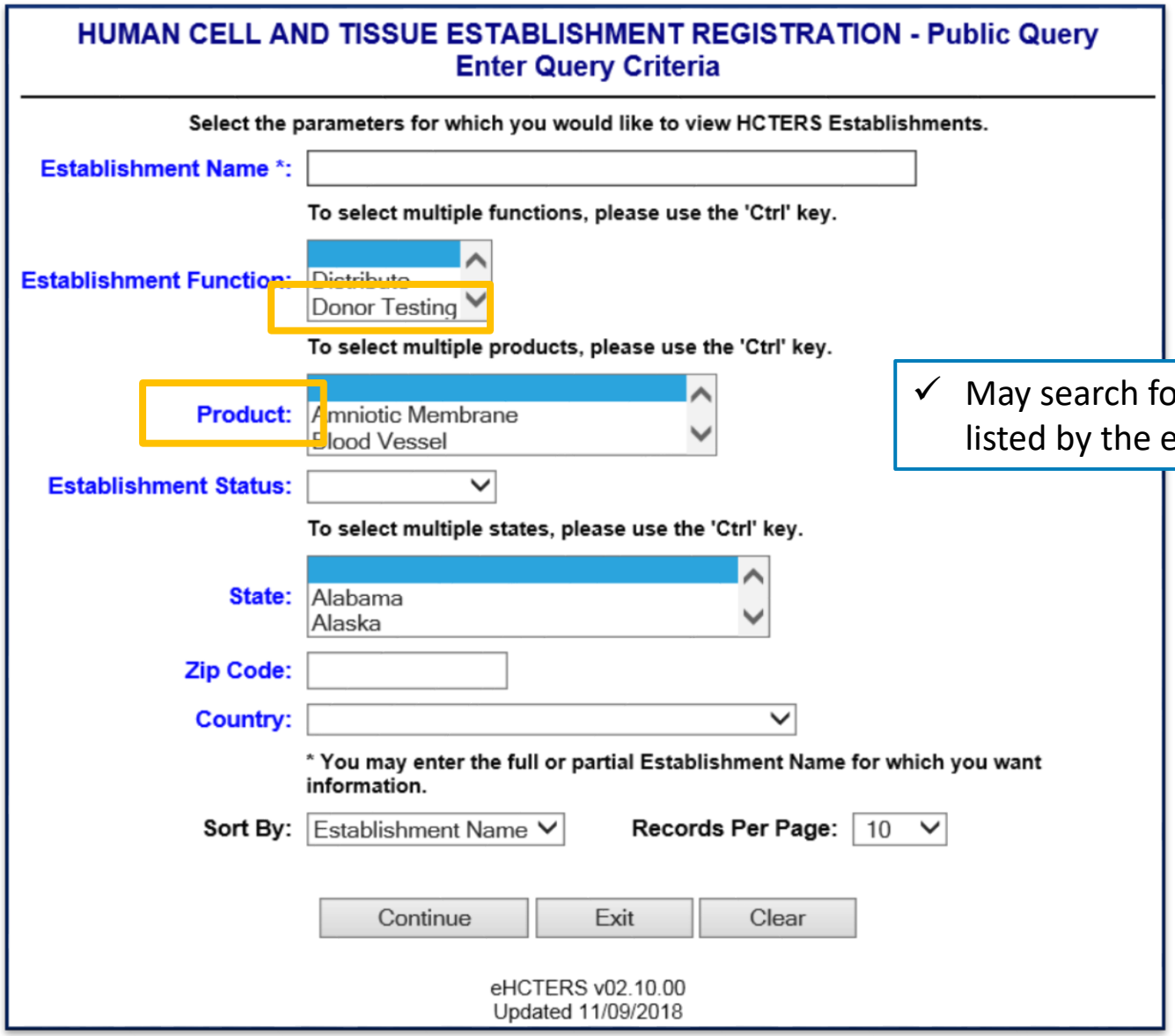
Public Query Application

Public Query

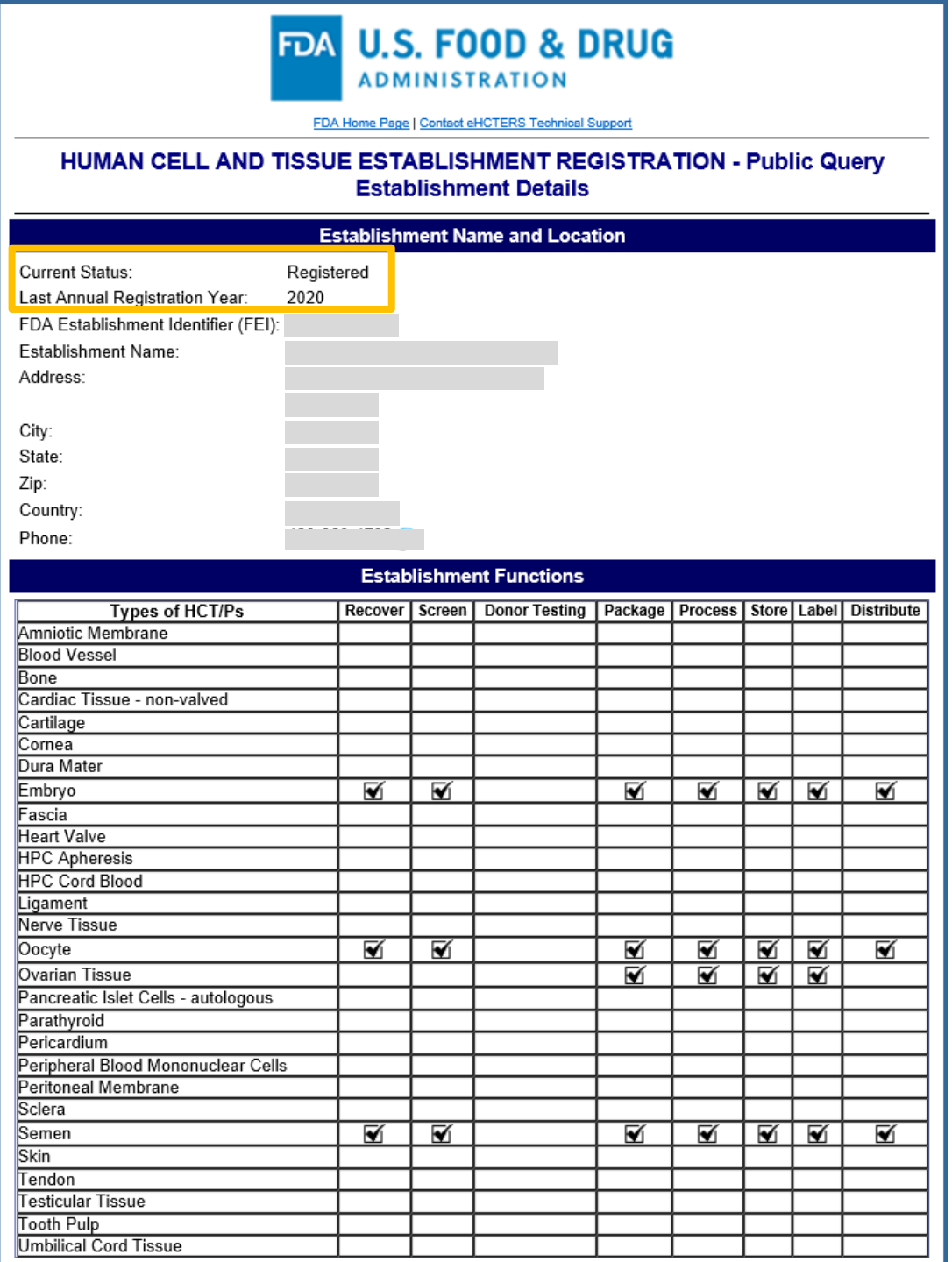
- Obtain information about HCT/P establishments and their registration status using the Human Cell and Tissue Establishment Registration Public Query application.

- FDA acceptance of an establishment's registration and HCT/P listing does not constitute a determination that an establishment is in compliance with applicable rules and regulations or that the HCT/P is licensed or approved by FDA (§ 1271.27(b)).

https://www.accessdata.fda.gov/scripts/cber/CFAppsPub/tiss/index.cfm



✓ May search for every HCT/P type listed by the establishment



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FDA Home Page | Contact eHCTERS Technical Support

HUMAN CELL AND TISSUE ESTABLISHMENT REGISTRATION - Public Query
Establishment Details

Establishment Name and Location

Current Status:	Registered
Last Annual Registration Year:	2020
FDA Establishment Identifier (FEI):	
Establishment Name:	
Address:	
City:	
State:	
Zip:	
Country:	
Phone:	

Establishment Functions

Types of HCT/Ps	Recover	Screen	Donor Testing	Package	Process	Store	Label	Distribute
Amniotic Membrane								
Blood Vessel								
Bone								
Cardiac Tissue - non-valved								
Cartilage								
Cornea								
Dura Mater								
Embryo	☑	☑		☑	☑	☑	☑	☑
Fascia								
Heart Valve								
HPC Apheresis								
HPC Cord Blood								
Ligament								
Nerve Tissue								
Oocyte	☑	☑		☑	☑	☑	☑	☑
Ovarian Tissue				☑	☑	☑	☑	
Pancreatic Islet Cells - autologous								
Parathyroid								
Pericardium								
Peripheral Blood Mononuclear Cells								
Peritoneal Membrane								
Sclera								
Semen	☑	☑		☑	☑	☑	☑	☑
Skin								
Tendon								
Testicular Tissue								
Tooth Pulp								
Umbilical Cord Tissue								

- ✓ Current Status:
  - Registered
  - Pre-registered (without FEI # assigned yet)
  - Inactive
- ✓ Last Annual Registration Year: indicates whether the establishment's registration is current.
  - e.g., "Last Annual Registration Year: 2020" means this registration expires on December 31, 2020.

Establishment HCT/P Listing

Types of HCT/Ps	HCT/Ps Described in 21 CFR 1271.10	Proprietary Names
Amniotic Membrane		
Blood Vessel		
Bone		
Cardiac Tissue - non-valved		
Cartilage		
Cornea		
Dura Mater		
Embryo	X	
Fascia		
Heart Valve		
HPC Apheresis		
HPC Cord Blood		
Ligament		
Nerve Tissue		
Oocyte	X	
Ovarian Tissue	X	
Pancreatic Islet Cells - autologous		
Parathyroid		
Pericardium		
Peripheral Blood Mononuclear Cells		
Peritoneal Membrane		
Sclera		
Semen	X	
Skin		
Tendon		
Testicular Tissue		
Tooth Pulp		
Umbilical Cord Tissue		

HCT/P Listing - Donor Information

Types of HCT/Ps	SIP	Directed	Anonymous	Autologous	Family Related
Embryo	☑	☑	☑		
HPC Apheresis					
HPC Cord Blood					
Oocyte	☑	☑	☑		
Peripheral Blood Mononuclear Cells					
Semen	☑	☑	☑		

Print Date: 03/23/2020

Print This Page | Back To Query Criteria Screen | Back To Query Results Screen

Exit

eHCTERS v02.11.00
Updated 10/25/2019

- ✓ Print Date is included on the page.

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Frequently Asked Questions

FAQ #1

Q1: My company performs manufacturing at multiple laboratories located in nearby buildings. Do I need to register and have an FEI number for each separate laboratory?

A: An establishment means a place of business under one management, at one general physical location, that engages in the manufacture of HCT/Ps (§ 1271.3(b)). One general physical location could be reasonably construed to include separate buildings within close proximity provided that the activities in them are closely related to the same business enterprise, under the supervision of the same local management, and capable of being inspected at the same time.

- For example, a hospital administrator could facilitate one registration of multiple laboratories under the same management. However, we recommend separate registrations for two or more business enterprises that are separate legal entities with different management even if both use the same facility or the same address.

FAQ #2

Q2: Do we need to register if we (IVF clinic) only receive and store cryopreserved semen for transfer into patients at our facility?

A: No — Exception in § 1271.15(d) applies: You are not required to comply with the requirements of this part if you are an establishment that does not recover, screen, test, process, label, package, or distribute, **but only receives or stores HCT/P's solely for implantation, transplantation, infusion, or transfer within your facility.**

Q2a: Does the answer change if we thaw & wash the semen before transfer into the recipient?

A: No — In this case, the clinic is the end user (consignee) and washing is considered part of preparation for transfer of the HCT/P.

FAQ #3

Q3: Do we need to register and list "Donor Testing" if we only obtain blood specimens from donors and send the specimens to a registered establishment (e.g., an independent laboratory or a recovery establishment) for testing?

A: No — If an individual or company is simply obtaining blood specimens from a donor and sending the blood specimens to a registered testing laboratory or to a registered recovery establishment, then the individual or company is not required to register. Obtaining blood specimens is not considered part of manufacturing.

FAQ #4

Q4: I'm importing gametes from a foreign establishment for use by a specific individual/couple. Does the foreign establishment need to register?

A: Yes. All foreign establishments importing or offering for import 361 HCT/Ps into the United States must register and list these HCT/Ps with CBER. Foreign establishments must provide information on their U.S. Agent(s) and Importers in accordance with § 1271.25(a)(5)-(6).

Tissue Registration Contact Information

Tissues Establishment Registration Webpage

https://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/EstablishmentRegistration/TissueEstablishmentRegistration/default.htm

Tissue Registration Coordinator

tissuereg@fda.hhs.gov

240-402-8369

Contact Information

- **Dan (Kelly) Wang**

  dan.wang@fda.hhs.gov
- **Regulatory Questions:**

  OTAT Main Line – 240 402 8190

  Email: OTATRPMS@fda.hhs.gov and

  Lori.Tull@fda.hhs.gov

FDA Headquarters

- **OTAT Learn Webinar Series:**

  http://www.fda.gov/BiologicsBloodVaccines/NewsEvents/ucm232821.htm

- **CBER website:** www.fda.gov/BiologicsBloodVaccines/default.htm
- **Phone:** 1-800-835-4709 or 240-402-8010
- **Consumer Affairs Branch**: ocod@fda.hhs.gov
- **Manufacturers Assistance and Technical Training Branch**: industry.biologics@fda.hhs.gov
- **Follow us on Twitter:** https://www.twitter.com/fdacber

THANK YOU

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