United States Food and Drug Administration

Human Cells, Tissues, and Cellular and Tissue-Based Products

OMB Control No. 0910-0543

SUPPORTING STATEMENT

Part A: Justification

1. Circumstances Making the Collection of Information Necessary

This information collection helps support Food and Drug Administration (FDA, we) implementation of statutory and regulatory requirements that govern certain human cells, tissues, and cellular and tissue-based products (HCT/Ps). Manufacturers of HCT/Ps regulated solely under the authority of section 361 of the Public Health Service Act (the PHS Act) (42 U.S.C. 264) are required to register and list HCT/Ps pursuant to part 1271 (21 CFR part 1271) whether or not the HCT/P enters into interstate commerce. Manufacturers of HCT/Ps regulated as drugs, devices and/or biological products under section 351 of the PHS Act (42 U.S.C. 262) and/or section 201 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321), are required to register and list HCT/Ps following the procedures in part 207 (21 CFR part 207) (if a drug and/or biological product) or part 807 (21 CFR part 807) (if a device). Information collection associated with the registration and listing requirements in parts 207 and 807 are currently approved in OMB control numbers 0910-0045 and 0910-0625, respectively.

Agency regulations in part 1271 set forth general provisions applicable to HCT/Ps in subpart A (§§ 1271.1 through 1271.20). Those HCT/Ps that are regulated solely under the authority of section 361 of the PHS Act are described in § 1271.10. Provisions in part 1271, subpart B (§§ 1271.21 through 1271.37), establish procedures for registration and listing including format and content elements along with scheduled timeframes for the submission of certain information and action by FDA. The regulations also provide for waivers from the electronic format requirement, amendments to establishment registration, and requesting information on registration and listing from FDA.

Registrants use Form FDA 3356, Establishment Registration and Listing for HCT/Ps, to submit HCT/P establishment registration and listing information to the Electronic Human Cell and Tissue Establishment Registration System (eHCTERS). Electronic submission of HCT/P establishment and product listing information is required under § 1271.22. However, a request for waiver of the electronic submission requirement may be submitted pursuant to § 1271.23. If the waiver request is granted, Form FDA 3356 (and accompanying instructions) may be downloaded to complete and submit by mail. The Tissue Establishment Registration page (https://www.fda.gov/vaccines-blood-biologics/biologics-establishment-registration/tissue-establishment-registration) provides access to eHCTERS, instructions for using eHCTERS, and other resource information that may be helpful to respondents.

Provisions in part 1271, subpart C (§§ 1271.45 through 1271.90), establish requirements for determining donor eligibility, including donor screening and testing, explaining these requirements are a component of current good tissue practice (CGTP) requirements set forth in part 1271, subpart D (§§ 1271.145 through 1271.320). The provisions in part 1271, subparts C and D, govern

the methods used in, and the facilities and controls used for, the manufacture of HCT/Ps, including, but not limited to all steps in recovery, donor screening, donor testing, processing, storage, labeling, packaging, and distribution.

The regulations in part 1271, subpart E and subpart F (§§ 1271.330 through 1271.440), establish additional requirements for establishments described in § 1271.10, including inspection and enforcement provisions, and recordkeeping requirements providing for the retention, notification to third parties, and disclosure of such records to FDA.

2. Purpose and Use of the Information Collection

We use the information received from establishments complying with registration and listing requirements to regulate the industries involved with the recovery, screening, testing, processing, storage, and distribution of HCT/Ps. The information allows FDA to efficiently and effectively handle emerging public health concerns related to HCT/Ps. The information also aids FDA to monitor the industry, to distribute educational materials, and to inform the industry about FDA requirements, guidances, and policies, and to identify entities that may be subject to FDA regulation.

Documentation of donor eligibility determination provides to the user that all of the donor's medical history and social behavior were reviewed for high risk for or clinical evidence of communicable diseases, and that all of the required testing was completed.

Other reporting and recordkeeping requirements in 21 CFR part 1271 are designed to fully disclose the screening and testing results to the user when using products from donors who are determined to be ineligible or whose eligibility has not yet been determined in an urgent medical need. The distributing establishment is also to document that the HCT/P establishment notified the physician that the screening and testing are not completed. HCT/P establishments are required to maintain records for a minimum of 10 years. Certain HCT/Ps have long storage periods and advances in medical diagnosis and therapy also have created opportunities for disease prevention or treatment many years after a recipient's exposure to a donor later determined to be at risk for communicable disease agents or diseases.

The CGTP information collection provisions provide: (1) additional measures for preventing the introduction, transmission, or spread of communicable disease; (2) step-by step consistency in the manufacturing of the product; (3) necessary information to FDA for the purpose of protecting public health and safety; (4) accountability in the manufacturing of cellular and tissue-based products; and (5) information facilitating the tracking of a product back to its original source or to a consignee or final disposition.

Without this collection of information, FDA could not monitor HCT/Ps procedures and could not fulfill its statutory responsibility to prevent the introduction, transmission, or spread of communicable diseases between the States or possessions or from foreign countries into the States.

3. Use of Improved Information Technology and Burden Reduction

Electronic submission of HCT/P establishment and product listing information is now required under §1271.22, unless waived in certain circumstances. HCT/P establishments that must register

and list electronically under 21 CFR Part 1271 should use eHCTERS (available at: https://www.accessdata.fda.gov/scripts/cber/CFApps/Login/Index.cfm) to meet the requirement for electronic submission of establishment registration and product listing. Establishments may request a waiver from the electronic submission requirement as described in §1271.23. With regard to recordkeeping, companies are free to use whatever forms of information technology may best assist them in retaining the appropriate records and making them available to regulatory officials. Our regulation at 21 CFR 1271.270(c) provides that establishments may maintain records electronically.

4. Efforts to Identify Duplication and Use of Similar Information

We are unaware of duplicative information collection. Manufacturers of drug or device products that incorporate human cells or tissues register using the FDA eHCTERS electronic system. To avoid duplication, 21 CFR parts 210, 211, and 820 state that in the event of a conflict between applicable regulations in parts 210, 211, and 820 and the regulations in part 1271, the regulation specifically applicable to the product in question must supersede the more general.

5. Impact on Small Businesses or Other Small Entities

The regulatory requirements apply to all respondents. The recordkeeping requirements are the minimum requirements for CGTP. To assist small businesses, FDA's Center for Biologics Evaluation and Research (CBER) provides industry guidance on its website and has established small business assistance contacts within its Office of Communication, Outreach, and Development (OCOD), Division of Manufacturer's Assistance and Training (DMAT), Manufacturers Assistance and Technical Training Branch (MATT) (email: Industry.Biologics@fda.hhs.gov).

6. Consequences of Collecting the Information Less Frequency

Information collection is consistent with statutory requirements. Less frequent collection of information would not provide FDA the information needed to prevent the transmission of communicable disease by HCT/Ps through monitoring, and communication with the cell and tissue industry. The documentation of donor eligibility, the summary of records, and the information provided to physicians on the donor's eligibility when a product is used in an urgent medical need is the minimum necessary to keep the industry informed of the eligibility of each and every donor of HCT/Ps. The reporting and recordkeeping requirements of CGTP are designed to impose minimum burden on industry while preventing the introduction, transmission, or spread of communicable disease through the use of HCT/Ps. There are no technical or legal obstacles to reducing the burden.

7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

The reporting regulations under 21 CFR part 1271, subparts C and D, require respondents to provide information more often than quarterly, i.e., for each individual HCT/P. This information includes an identification code number, which protects patient/donor confidential information.

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

In the *Federal Register* of April 19, 2023 (88 FR 24193), FDA published a 60-day notice requesting public comment on the proposed extension of this collection of information. FDA received one comment in response to the notice. The comment was outside the scope of the four collection of information topics on which the notice solicited comments.

9. Explanation of Any Payment or Gift to Respondents

There are no incentives, payments or gifts associated with this information collection.

10. Assurance of Confidentiality Provided to Respondents

In preparing this Supporting Statement, we consulted our Privacy Office to ensure appropriate identification and handling of information collected.

This ICR collects personally identifiable information (PII). PII is collected in the context of the subject individuals' professional capacity and the FDA-related work they perform for their employer (e.g., point of contact at a regulated entity). The PII submitted via the e-Submission (eHCTERS) system is username, password, name, mailing address, email address, and telephone number. FDA determined that although PII is collected, the collection is not subject to the Privacy Act of 1974 and the particular notice and other requirements of the Privacy Act do not apply. Specifically, FDA does not use name or any other personal identifier to retrieve records from the information collected. Through appropriate guidance, FDA limited submission fields and minimized the PII collected to protect the privacy of the individuals.

Under the Freedom of Information Act (FOIA) (5 U.S.C. 552), the public has broad access to government documents. However, FOIA provides certain exemptions from mandatory public disclosure of government records (5 U.S.C. 552(b)(1-9)). FDA will make the fullest possible disclosure of records to the public, consistent with the rights of individuals to privacy, the property rights of persons in trade and confidential commercial or financial information.

Confidential commercial information is also protected by Section 301(j) of the FD&C Act; and, by part 20 of our regulations (21 CFR part 20).

11. Justification for Sensitive Questions

Questions of a sensitive nature, such as sexual behavior and other matters that are commonly considered private must be asked by the HCT/P establishments as part of the donor medical history evaluation. The answers to these questions help determine the eligibility of a donor. Donors that do not meet certain criteria would be determined ineligible to donate. This information is necessary to prevent the transmission of relevant communicable diseases and to protect the public health. Such information may be reviewed by FDA during an inspection.

12. Estimates of Annualized Burden Hours and Cost

12a. Annualized Hour Burden Estimate

Description of Respondents: Respondents to this information collection are establishments that recover, process, store, label, package, or distribute any HCT/P that is regulated solely under section 361 of the PHS Act and regulations in part 1271 or perform donor screening or testing.

We estimate the burden of the information collection as follows:

Table 1.--Estimated Annual Reporting Burden

21 CFR Section; Reporting Activities	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours[2]
1271.10(b)(1) and 1271.21(b)[1]; register and submit list of each HCT/P manufactured by existing establishments	2,374	1	2,374	0.5 (30 minutes)	1,187
1271.10(b)(1) and (2), 1271.21(a), and 1271.25(a) and (b)[1]; register and submit list of each HCT/P manufactured by new establishments	157	1	157	0.75 (45 minutes)	118
1271.10(b)(2), 1271.21(c)(ii), and 1271.25(c)[1]; update list	566	1	566	0.5 (30 minutes)	283
1271.23; request electronic format waiver	1	1	1	1	1
1271.26[1]; location/ownership amendments	346	1	346	0.25 (15 minutes)	87
1271.155(a); request exemption or alternative to any requirement	18	1.333	24	3	72
1271.350(a)(1) and (3); investigate and report adverse actions	15	14.266	214	1	214
1271.420(a); notify FDA (imports)	200	2.8	560	0.25 (15 minutes)	140
Total		23.399	4,242		2,102

[1] Using eHCTERS.

[2] Rounded to the nearest whole number.

Based on current data from eHCTERS, we estimate there are 2,374 HCT/P current registrants and 157 new registrants, for a total of 2,531 respondents annually. Information collection provisions that include reporting activities are identified in table 1. The estimated burden for each of the individual reporting activities was calculated based on the annual number of submissions, averaged among respondents, and based on informal communications with industry.

Table 2.--Estimated Annual Recordkeeping Burden

21 CFR Part 1271; Establish and Maintain Records	No. of Recordkeepers	No. of Records per Recordkeeper[2]	Total Annual Records	Average Burden per Recordkeeping[1]	Total Hours[2]
1271.47; Establishing SOPs	157	1	157	48	7,536
1271.47; Updating SOPs	2,374	1	2,374	24	56,976
1271 Subpart C & Subpart	2,531	3,311.36	8,381,049	0.26	2,170,493

D: Establishing and maintaining records documenting methods used in, and the facilities and controls used for, the manufacture of HCT/Ps, including but not limited to all steps in recovery, donor screening, donor testing, processing, storage, labeling, packaging, and distribution				(~15 minutes)	
Total			8,383,580		2,235,005

[1] Decimals rounded to the nearest hundredth.

[2] Rounded to the nearest whole number.

To calculate burden associated with the establishment and maintenance of operating procedures in accordance with applicable CGTP requirements, we assume twice the time is necessary for new establishments. Burden we attribute to recordkeeping activities associated with the remaining provisions in part 1271 is assumed to be distributed among the individual elements and averaged among respondents.

Table 3.--Estimated Annual Third-Party Disclosure Burden

21 CFR Part 1271--Human Cells, Tissues, and Cellular and Tissue-Based Products; Activity	No. of Respondents	No. of Disclosures per Respondent[2]	Total Annual Disclosures	Average Burden per Disclosure[1]	Total Hours
Disclosing information as required under applicable good manufacturing practices/CGTP provisions	1,611	4,984.75	8,030,435	0.30 (~18 minutes)	2,389,226

[1] Decimals rounded to the nearest hundredth.

As part of the recordkeeping requirements, certain provisions in part 1271 require the disclosure of information to third parties, particularly as it pertains to the distribution of HCT/Ps. We estimate a proportion of the respondents to the information collection (1,611) will incur burden resulting from these disclosures and have therefore accounted for burden that may be attributable to these distinct activities.

12b. Annualized Cost Burden Estimate

The estimated annual cost to respondents is $267,186,570.00.

Activity	No. of Hours	Cost per Hour	Total Cost
Reporting	2,102	$65	$136,630
Recordkeeping	2,235,005	$50	111,750,250

Disclosure	2,389,226	$65	$155,299,690
Total			$267,186,570

The reporting/disclosure cost estimate is based on an average pay rate of $65 an hour. The average is based on the salaries of a medical director ($94/hour), a mid-level supervisor ($60/hour, responsible for completing and submitting the registration and/or listing information; creating, reviewing, or updating SOPs; or on other reporting responsibilities), and a medical technician ($40/hour). The recordkeeping cost estimate is based on an average pay rate of $50/hour of a mid-level professional and a medical technician who are involved with the documentation and maintenance of records. The estimated average hourly pay rate includes benefits but no overhead costs.

13. Estimates of Other Total Annual Costs to Respondents/Recordkeepers or Capital Costs

There are no capital, start-up, operating or maintenance costs associated with this collection of information.

14. Annualized Cost to the Federal Government

The estimated annualized cost to FDA is $ 4,406,247.00.

Activity	Number of Responses	Hours per Response	Cost per Hour	Total Cost
Registration and Listing	3,443	3	$50	$516,450
Exemption or Alternative Request	24	3	$78	$5,616
Establishment (non-reproductive) Inspection	790	69	$67	$3,652,170
Establishment (reproductive) Inspection	199	17	$67	$226,661
AER triage/review	214	0.5 (30 mins)	$50	$5,350
Total				$4,406,247

The estimated cost is based on 2 FTEs (GS-7/5 and GS-13/5), with an average pay rate of $50 an hour, who process and review the registration form, input the data, and maintain the database; and who triage and review AERs. There are approximately 1,579 non-reproductive HCT/P establishments that would be inspected on a biennial basis (1,579/2 = 790) by a FDA Inspector at an average grade of GS-13/5, with an average pay rate of $67 an hour. The estimated time includes inspection, reviewing records and writing up a report. There are approximately 795 (2,374 – 1,579 = 795) reproductive HCT/P establishments that would be inspected for compliance with the donor eligibility requirements every 4 years (795/4 =199) per year). This cost is also based on FDA regulatory review staff who process and review the requests for exemptions or alternatives, with an average pay rate of $78 an hour. The salary estimates include benefits but no overhead costs.

15. Explanation for Program Changes or Adjustments

Our estimated burden for the information collection reflects an overall reduction of 150,137 hours and 347,843 responses annually. We attribute this adjustment to a decrease in the number of HCT/P establishments and a decrease in the number of HCT/Ps distributed since our last evaluation.

16. Plans for Tabulation and Publication and Project Time Schedule

The information collected will not be published or tabulated. However, the public may review tissue establishment registration information for registered, inactive, and pre-registered establishments by using the eHCTERS Public Query application available at: https://www.accessdata.fda.gov/scripts/cber/CFAppsPub/tiss/Index.cfm.

17. Reason(s) Display of OMB Expiration Date is Inappropriate

FDA is not seeking approval to exempt the display of the expiration date of the OMB Approval. We intend to add a link to the public protection information in the next release to maximize cost effectiveness of the IT updates. By including in the next release, the change will not generate an additional contract item.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.