UNITED STATES FOOD AND DRUG ADMINISTRATION

Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps):
Establishment Registration and Listing;
Eligibility Determination for Donors;
and Current Good Tissue Practice (CGTP)

OMB Control No. 0910-0543

SUPPORTING STATEMENT – **Part A: Justification**

1. Circumstances Making the Collection of Information Necessary

This information collection supports Food and Drug Administration (FDA, us or we) regulations related to human cells, tissues, and cellular and tissue-based products (HCT/Ps). Under the Federal Food, Drug, and Cosmetic Act (FD&C Act) and section 361 of the Public Health Service Act (the PHS Act) (42 U.S.C. 264), FDA may issue and enforce regulations necessary to prevent the introduction, transmission, or spread of communicable diseases between the States or possessions or from foreign countries into the States. As derivatives of the human body, all HCT/Ps pose some risk of carrying pathogens that could potentially infect recipients or handlers. Accordingly, our regulations in 21 CFR part 1271 govern HCT/Ps electronic establishment registration and listing using an electronic system, eligibility determination for donors, and current good tissue practice (CGTP). The regulations are necessary to prevent the introduction, transmission, or spread of communicable diseases. We therefore request extension of OMB approval of the information collection provisions found in 21 CFR part 1271, as well as the Electronic Human Cell and Tissue Establishment Registration System (eHCTERS), as discussed in this supporting statement.

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. Each distributed HCT/P must have the following accompanying documentation: (1) a distinct identification code; (2) a statement, based on the screening and testing results, that the donor is determined to be eligible or ineligible; and (3) a summary of the records used to determine eligibility. The summary of records must contain: (1) a statement that the testing was performed by a Clinical Laboratory Improvement Amendments certified laboratory or by a laboratory that has met

equivalent requirements as determined by the Centers for Medicare and Medicaid Services; (2) a listing and interpretation of the results of all communicable disease tests performed; (3) the name and address of the establishment determining the eligibility of the donor; and (4) in the case of an HCT/P from a donor determined to be ineligible based on screening and released for use under § 1271.65(b), a statement noting the reason for the ineligible determination.

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 accordance with 5 CFR 1320.8(d), FDA published a 60-day notice for public comment in the *Federal Register* of December 5, 2019 (84 FR 66673). No comments were received.

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 handling of information collected. The information collection captures personally identifiable information (PII) or information of a personal nature including name, mailing address, email address, and telephone number. PII is collected in the context of the individual's professional capacity. We have determined, however, that the PII collected is not subject to the Privacy Act of 1974 and the particular notice and other requirements of the Act do not apply. Specifically, FDA does not use name or any other personal identifier to routinely retrieve records from the information collected. Inspectors may copy records as part of the inspection of a tissue establishment. Establishment records describing manufacturing procedures and CGTP records that we may copy or take possession of during an inspection often contain trade secret and confidential commercial information. Confidential commercial information is protected from disclosure under the Freedom of Information Act (FOIA) under sections 552(a) and (b) (5 U.S.C. 552(a) and (b)); 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. Annualized Burden Estimate

12a. Annualized Burden Estimate

Table 1.--Estimated Annual Reporting Burden[1]

21 CFR Part 1271; Human Cells, Tissues, and Cellular and Tissue-Based Products	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours[3]
1271.10(b)(1) and 1271.21(b)[2]	2,736	1	2,736	0.5 (30 minutes)	1,368
1271.10(b)(1) and (2), 1271.21(a), and 1271.25(a) and (b)[2]	193	1	193	0.75 (45 minutes)	145
1271.10(b)(2), 1271.21(c)(2)(ii) and 1271.25(c)[2]	1,062	1	1,062	0.5 (30 minutes)	531
1271.23	1	1	1	1	1
1271.26[2]	358	1	358	0.25 (15 minutes)	90
1271.155(a)	15	4.27	64	3	192
1271.350(a)(1) and (3)	13	14.46	188	1	188
1271.420(a)	200	2.8	560	0.25	140

21 CFR Part 1271; Human Cells, Tissues, and Cellular and Tissue-Based Products	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours[3]
				(15 minutes)	
			5,162		2,655

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.
[2] Using eHCTERS.
[3] Rounded to the nearest whole number.

Table 2.--Estimated Annual Recordkeeping Burden[1]

21 CFR Part 1271; Human Cells, Tissues, and Cellular and Tissue-Based Products	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours[3]
New SOPs[2]	193	1	193	48	9,264
SOP Update[2]	2,736	1	2,736	24	65,664
1271.47(d)	1,368	1	1,368	1	1,368
1271.50(a)	2,736	39.846	109,019	5	545,095
1271.55(d)(1)	2,736	39.846	109,019	1	109,019
1271.55(d)(2)	2,736	1	2,736	1	2,736
1271.55(d)(4)	2,736	1	2,736	120	328,320
1271.60(d)(3) and (4) 1271.65(b)(3)(iii)	821	1	821	2	1,642
1271.155(f)	15	4.27	64	0.25 (15 minutes)	16
1271.160(b)(3) and (6)	2,109	12	25,308	1	25,308
1271.160(d)	2,109	12	25,308	1	25,308
1271.190(d)(2)	2,109	12	25,308	1	25,308
1271.195(d)	2,109	12	25,308	1	25,308
1271.200(e)	2,109	12	25,308	1	25,308
1271.210(d)	2,109	12	25,308	1	25,308
1271.230(a)	2,109	12	25,308	1	25,308
1271.230(c)	2,109	1	2,109	1	2,109
1271.260(d)	2,109	12	25,308	0.25 (15 minutes)	6,327
1271.260(e)	2,109	365	769,785	0.083 (5 minutes)	63,892
1271.265(c)(1)	2,109	1,163.781	2,454,415	0.083 (5 minutes)	203,716
1271.265(c)(3)	1,055	1	1,055	1	1,055
1271.265(e)	2,109	1,163.781	2,454,415	0.083 (5 minutes)	203,716
1271.270(a)	2,109	1,163.781	2,454,415	0.25 (15 minutes)	613,604
1271.270(e)	2,189	2	4,378	0.5 (30 minutes)	2,189
1271.290(d) and (e)	2,109	49.037	103,419	0.25 (15 minutes)	25,855
1271.320(b)	1,687	5	8,435	1	8,435
			8,683,582		2,371,178

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.

[2] Sections 1271.47(a), 1271.85(b)(2), 1271.160(b)(2) and (d)(1), 1271.180(a), 1271.190(d)(1), 1271.200(b), 1271.200(c), 1271.230(a), 1271.250(a), and 1271.265(e).
[3] Rounded to the nearest whole number.

Table 3.--Estimated Annual Third-Party Disclosure Burden[1]

21 CFR Part 1271; Human Cells, Tissues, and Cellular and Tissue-Based Products	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
1271.55(a)	1,632	1,589.715	2,594,415	0.5 (30 minutes)	1,297,208
1271.60(c) and (d)(2)	1,611	355.06	572,000	0.5 (30 minutes)	286,000
1271.290(c)	2,109	1,163.781	2,454,415	0.083 (5 minutes)	203,716
1271.290(f)	2,109	1	2,109	1	2,109
1271.370(b) and (c)	2,109	1,163.781	2,454,415	0.25 (15 minutes)	613,604
Total	9,570		8,077,354		2,402,637

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.
[2] Rounded to the nearest whole number.

12b. Annualized Cost Estimate

The estimated annual cost to respondents is $234,354,056.00.

Activity	No. of Hours	Cost per Hour	Total Cost
Reporting	2,655	$58	$153,990
Recordkeeping	2,371,178	$40	$94,847,120
Disclosure	2,402,637	$58	$139,352,946
Total			$234,354,056

The reporting/disclosure cost estimate is based on an average pay rate of $58 an hour. The average is based on the salaries of a medical director ($85/hour), a mid-level supervisor ($54/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 ($36/hour). The recordkeeping cost estimate is based on an average pay rate of $44/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 and/or Recordkeepers/Capital Costs

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

14. Cost to the Federal Government

The estimated annualized cost to FDA is $5,195,140.00.

Activity	Number of Responses	Hours per Response	Cost per Hour	Total Cost
Registration and Listing	4,349	3	$44	$574,068
Exemption or Alternative Request	64	3	$71	$13,632
Establishment (non-reproductive) Inspection	1,055	69	$61	$4,440,495
Establishment (reproductive) Inspection	157	17	$61	$162,809
AER triage/review	188	0.5 (30 mins)	$44	$4,136
Total				$5,195,140

The estimated cost is based on 2 FTEs (GS-7/5 and GS-13/5), with an average pay rate of $44 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 2,109 non-reproductive HCT/P establishments that would be inspected on a biennial basis (2,109/2 = 1,055) by a FDA Inspector at an average grade of GS-13/5, with an average pay rate of $61 an hour. The estimated time includes inspection, reviewing records and writing up a report. There are approximately 627 (2,736 – 2,109 = 627) reproductive HCT/P establishments that would be inspected for compliance with the donor eligibility requirements every 4 years (627/4 =157) 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 $71 an hour. The salary estimates include benefits but no overhead costs.

15. Explanation for Program Changes or Adjustments

The information collection reflects adjustments. We have increased the number of respondents based on the number of registered establishments. We have also incorporated burden from electronic registration requirements now mandatory as a result of final rule RIN 0910-AA49. This results in an overall increase in annual responses by 2,584,285 but reduces the annual hours by 4,559,578.

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.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.