Food and Drug Administration
Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps):
Establishment Registration and Listing; Form FDA 3356;
Eligibility Determination For Donors;
and Current Good Tissue Practice (CGTP)
OMB Control No. 0910-0543
Supporting Statement

A. Justification

1. Circumstances Making the Collection of Information Necessary

The information collection supports agency regulations. Under the Federal Food, Drug, and Cosmetic Act (the FFDCA) and section 361 of the Public Health Service Act (the PHS Act)(42 U.S.C. 264), the Food and Drug Administration (FDA) has promulgated regulations at 21 CFR Part 1271 regarding human cells, tissues, and cellular and tissue-based products including requirements for the registration and listing by manufacturers of these products. The regulations also establish donor-eligibility as well as Current Good Tissue Practice, and are intended to prevent the transmission and spread of communicable disease. Accordingly, FDA is requesting approval of the information collection provisions found in 21 CFR Part 1271 as identified and discussed below. We are also requesting the approval of associated Form FDA 3356 entitled, "*ESTABLISHMENT REGISTRATION AND LISTING FOR HUMAN CELLS, TISSUES, AND CELLULAR AND TISSUE-BASED PRODUCTS (HCT/Ps)"* Form FDA 3356 has been revised consistent with current rulemaking (81 FR 60170, approved under OMB Control No. 0910-0829) as follows: (1) Adding import contact information including an email address and phone number; (2) deleting columns related to HCT/Ps subject to registration and listing under 21 CFR part 207 or 807; and (3) revising the instructions accordingly.

2. Purpose and Use of the Information Collection

The information FDA receives from establishments complying with registration and listing requirements is necessary 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 ensure that communicable diseases are not spread into or throughout the United States and its Possessions.

3. Use of Improved Information Technology and Burden Reduction

FDA has developed Form FDA 3356 which may be submitted electronically through a secure web server or in paper form by mail or FAX. Establishments may maintain records electronically or as original paper records, or as true copies such as photocopies, microfiche, or microfilm. Electronic recordkeeping is specifically referred to in the regulations under § 1271.270(c). Advanced methods of recordkeeping, e.g., by an electronic method, have improved the ability of HCT/P establishments to more easily maintain and retrieve records of donor eligibility determinations, and CGTP.

4. Efforts to Identify Duplication and use of Similar Information

Manufacturers of drug or device products that incorporate human cells or tissues register only using Form FDA 3356. 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. We are otherwise unaware of any potential duplicative information collection.

5. Impact on Small Businesses or Other Small Entities

The regulatory requirements apply to all respondents. To assist small businesses, FDA provides industry guidance on its website and has established small business assistance contacts throughout the agency including the Office of Communications, Outreach, and Development, Division of Manufacturer's Assistance and Training within FDA's Center for Biologics Evaluation and Research (CBER).

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 burden 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 September 7, 2016 (81 FR 61685). No comments were received. Also, in the Federal Register of August 31, 2016, FDA finalized its rule entitled, "*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*" revising the information collection. No comments were received regarding the information collection provisions.

9. Explanation of Any Payment or Gift to Respondents

No payment or gift was provided to respondents.

10. Assurance of Confidentiality provided to respondents

The confidentiality of information received by FDA would be consistent with the Freedom of Information Act (FOIA) and FDA's published regulations of "Public Information" under 21 CFR

Part 20. Inspectors may copy records as part of the inspection of a tissue establishment. This information is for internal use and may be subject to, in whole or in part, the FOIA and applicable FDA regulations.

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

We estimate the burden of the information collection as follows:

Table 1- Estimated Annual Reporting Burden[1]

21 CFR Section	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Avg. Burden per Response	Total Hours[3]
1271.10(b)(1) and 1271.21(b)[2]	2,218	1	2,218	.5 (30 mins)	1,109
1271.10(b)(1) and (b)(2), 1271.21(a), and 1271.25(a) and (b)[2]	182	1	182	.75 (45 mins)	137
1271.10(b)(2), 1271.21(c)(2)(ii) and 1271.25(c)[2]	1,221	1	1,221	.5 (30 mins)	611
1271.26[2]	588	1	588	.25 (15 mins)	147
1271.155(a)	25	3.12	78	3	234
1271.350(a)(1) and (a)(3)	34	4.88	166	1	166
1271.420(a)	200	2.8	560	.25 (15 mins)	140
Total					2,544

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

[2] Using Form FDA 3356.

[3] Rounded to the nearest whole number.

Table 2 – Estimated Annual Recordkeeping Burden[1]

21 CFR Section	No. of Record-keepers	No. of Records per Recordkeeper	Total Annual Records	Avg. Burden per Recordkeeping	Total Hours[3]
New SOPs[2]	182	1	182	48	8,736
SOP Update[2]	2,218	1	2,218	24	53,232
1271.47(d)	1,109	1	1,109	1	1,109
1271.50(a)	2,218	49.15	109,019	5	545,095
1271.55(d)(1)	2,218	49.15	109,019	1	109,019
1271.55(d)(2)	2,218	1	2,218	1	2,218
1271.55(d)(4)	2,218	1	2,218	120	266,160
1271.60(d)(3) and (d)(4) 1271.65(b)(3)(iii)	665	1	665	2	1,330
1271.155(f)	25	3.12	78	.25 (15 minutes)	20
1271.160(b)(3) and (b)(6)	1,561	12	18,732	1	18,732
1271.160(d)	1,561	12	18,732	1	18,732
1271.190(d)(2)	1,561	12	18,732	1	18,732
1271.195(d)	1,561	12	18,732	1	18,732
1271.200(e)	1,561	12	18,732	1	18,732
1271.210(d)	1,561	12	18,732	1	18,732
1271.230(a)	1,561	12	18,732	1	18,732
1271.230(c)	1,561	1	1,561	1	1,561
1271.260(d)	1,561	12	18,732	.25 (15 minutes)	4,683
1271.260(e)	1,561	365	569,765	.083 (5 minutes)	47,291
1271.265(c)(1)	1,561	1,324.08	2,066,890	.083 (5 minutes)	171,552
1271.265(c)(3)	781	1	781	1	781
1271.265(e)	1,561	1,324.08	2,066,890	.083 (5 minutes)	171,552
1271.270(a)	1,561	1,324.08	2,066,890	.25 (15 minutes)	516,723
1271.270(e)	1,774	2	3,548	.5 (30 minutes)	1,774
1271.290(d) and (e)	1,561	66.25	103,419	.25 (15 minutes)	25,855
1271.320(b)	1,249	5	6,245	1	6,245
Total					2,066,060

[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), 1271.265(e), 1271.265(f), 1271.270(b) and (d), 1271.290(b)(1), and 1271.320(a).

[3] Rounded to the nearest whole number.

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

21 CFR Section	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
1271.55(a)	1,551	1,422.88	2,206,890	.5 (30 minutes)	1,103,445
1271.60(c) and (d)(2)	1,375	416	572,000	.5 (30 minutes)	286,000
1271.290(c)	1,561	1,324.08	2,066,890	.083 (5 minutes)	171,552
1271.290(f)	1,561	1	1,561	1	1,561
1271.370(b) and (c)	1,561	1,324.08	2,066,890	.25 (15 minutes)	516,723
Total					2,079,281

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

12b. Annualized Cost Estimate

The estimated annual cost to respondents is $201,274,895.00.

Activity	No. of Hours	Cost per Hour	Total Cost
Reporting	2,544	$55	$139,920
Recordkeeping	2,066,060	$42	$86,774,520
Disclosure	2,079,281	$55	$114,360,455
Total			$201,274,895

The reporting/disclosure cost estimate is based on an average pay rate of $55 an hour. The average is based on the salaries of a medical director ($80/hour), a mid-level supervisor ($51/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 ($34/hour). The recordkeeping cost estimate is based on an average pay rate of $42/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 costs or operating and maintenance costs associated with this collection of information.

14. Cost to the Federal Government

The estimated annualized cost to FDA is $3,906,619.00.

Activity	Number of Responses	Hours per Response	Cost per Hour	Total Cost
Registration and Listing	4,209	3	$43	$542,961
Exemption or Alternative Request	78	3	$69	$16,146
Establishment (non-reproductive) Inspection	781	69	$59	$3,179,451
Establishment (reproductive) Inspection	164	17	$59	$164,492
AER triage/review	166	1/2 (30 mins)	$43	$3,569
Total				$3,906,619

The estimated cost is based on 2 FTEs (GS-7/5 and GS-13/5) who process and review the registration form, input the data, and maintain the database; and who triage and review AERs. There are approximately 1,561 non-reproductive HCT/P establishments that would be inspected on a biennial basis (1,561/2 = 781) by a FDA Inspector at an average grade of GS-13/5. The estimated time include inspection, reviewing records and writing up a report. There are approximately 657 (2,218 – 1,561 = 657) reproductive HCT/P establishments that would be inspected for compliance with the donor eligibility requirements every 4 years (164 (657/4) per year). This cost is also based on FDA regulatory review staff who process and review the requests for exemptions or alternatives. The salary estimates include benefits but no overhead costs.

15. Explanation for Program Changes or Adjustments

The agency has adjusted its estimate to reflect an increase of 509,539 in annual responses and 5,397,434 in annual hours. We attribute the change to an increase in third party disclosures and the addition of nominal burden approved under OMB Control No. 0910-0829 resulting from rulemaking (an increase of 4,225 responses and 1,919 hours from revised registration and listing requirements).

16. Plans for Tabulation and Publication and Project Time Schedule

The agency has no such plans.

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

Display of OMB expiration date is appropriate.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.