U.S. Food and Drug Administration
Guidance on Informed Consent For In Vitro Diagnostic Device Studies Using Leftover Human Specimens That Are Not Individually Identifiable

0910-0582
SUPPORTING STATEMENT

Terms of Clearance: None.

A. Justification

1. Circumstances Making the Collection of Information Necessary

This information collection supports Food and Drug Administration (FDA, us or we) guidance. The Food and Drug Administration has notified the public in a guidance document of the circumstances in which it intends to exercise enforcement discretion as to the informed consent regulations (as required by section 520(g) of the Federal Food, Drug, and Cosmetic Act and 21 CFR part 50) for *in vitro* diagnostic device studies that are conducted using leftover specimens and that meet the criteria for exemption from the Investigational Device Exemption (IDE) regulation at 21 CFR 812.2(c)(3), as long as subject privacy is protected by using only specimens that are not individually identifiable.

In the guidance document, entitled "Informed Consent For In Vitro Diagnostic Device Studies Using Leftover Human Specimens That Are Not Individually Identifiable," FDA recommends that sponsors of studies that meet the factors/circumstances described in the guidance maintain documentation of how these factors were met and of the types of human subject protection procedures followed by the specimen provider to ensure that the subject cannot be identified. The agency developed this guidance because it became aware that the requirement to obtain informed consent for IVD studies (including those using leftover human specimens) was bringing to a halt a class of very valuable investigations used to evaluate the performance of potentially valuable diagnostic tests. FDA believes these requirements do not, in the circumstances described above, appreciably add protection for human subjects, which is the purpose of having informed consent requirements in the first place.

The agency included this recordkeeping in the guidance document because IVD manufacturers that embrace this enforcement discretion policy should have documentation to demonstrate that their product met the factors/circumstances described in the guidance.

The guidance refers to previously approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in 21 CFR 812.2(c)(3), regarding "Investigational Device Exemptions Reports and Records," have been approved under OMB control number 0910-0078. Additionally, the collections of information in 21 CFR

part 56.115, “Protection of Human Subjects; Recordkeeping Requirements for Institutional Review Boards,” have been approved under OMB control number 0910-0130.

2. Purpose and Use of the Information Collection

FDA has announced the availability of a guidance entitled, “Guidance on Informed Consent for *In Vitro* Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable.” The guidance defines when the agency intends to exercise enforcement discretion regarding informed consent requirements (21 CFR part 812.50) with regard to leftover human specimens that are not individually identifiable that are used in certain *in vitro* diagnostic studies.

The guidance document recommends that sponsors (investigators, IVD manufacturers or federal government agencies that develop and evaluate IVD tests) that meet the factors described in the guidance maintain records of how these factors were met. Sponsors that wish to take advantage of this policy will substitute use of records to demonstrate conformance to this enforcement discretion policy in place of the more detailed and patient specific records for obtaining and documenting informed consent. Most fundamentally, this means collecting and maintaining information about the protections that are in place to prevent the identification of the specimens, because making sure that the specimens are not identifiable is key to obtaining FDA's enforcement discretion.

FDA intends to exercise enforcement discretion when all of the following are true:

- the investigation meets the IDE exemption criteria at 21 CFR 812.2(c)(3);
- the study uses leftover specimens, that is, remnants of specimens collected for routine clinical care or analysis that would have been discarded. The study may also use specimens obtained from specimen repositories or leftover specimens that were previously collected for other research purpose may also be used;
- the specimens are not individually identifiable;
- the specimens may be accompanied by clinical information as long as this information does not make the specimen source identifiable to the investigator or any other individual associated with the investigation, including the sponsor;
- the individuals caring for the patients are different from and do not share information with those conducting the investigation;
- the specimens are provided to the investigator(s) without identifiers and the supplier of the specimens has established policies and procedures to prevent the release of personal information; and
- the study has been reviewed by an IRB in accordance with 21 CFR part 56.

3. Use of Improved Information Technology and Burden Reduction

Companies are free to use whatever forms of information technology may best assist them in utilizing this guidance document. FDA estimates that 95% of the respondents will use electronic means to fulfill the agency’s requirement or request.

4. Efforts to Identify Duplication and Use of Similar Information

As this is a guidance document, no firm is required by regulation to take advantage of this policy. There should be no duplicative information collection as a result of this guidance.

5. Impact on Small Businesses or Other Small Entities

   This guidance document offers clinical investigators and sponsors (including small businesses) a pathway for using leftover human specimens that are not individually identifiable (short forms are not applicable). This will be an alternative to existing requirements for sponsors to obtain informed consent, which could be extraordinarily time-consuming and costly, if not impossible. This pathway was not previously available; thus the policy expressed in the guidance document should help facilitate important research in a cost-effective way. FDA estimates that 70% of respondents are small businesses.

6. Consequences of Collecting the Information Less Frequently

   This guidance may reduce the information collection burden on clinical investigators and sponsors by requesting only that they meet the factors in the guidance, rather than keeping the records and satisfying other information collection requirements related to obtaining informed consent (the collections of information in 21 CFR 812.2(c)(3) have been approved under OMB control number 0910-0078). The clinical investigators and sponsors need to maintain written documentation demonstrating that they meet the factors in the guidance only if they choose to take advantage of the policy expressed in the guidance. Respondents will respond to the data collection only once per investigation.

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

   There are no special circumstances for this collection of 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 March 5, 2019 (84 FR 7906). FDA received the following comments:

   Comment: Some comments strongly support further harmonization between the updated Common Rule and FDA regulations. Although the comments support the FDA's 2006 Guidance and discretionary enforcement, the comments suggested that scientists would welcome expanded efforts to remove investigations using de-identified human tissues from FDA's human subject regulations, consistent with the Common Rule. The comments suggest there is little practical utility in FDA maintaining de-identified specimens as part of human subject investigations. The comments suggest that removing de-identified specimens from these requirements would allow for safety and ethical considerations while reducing administrative burden for investigators, ensuring consistency with the Common Rule and streamlining effectiveness. The comments suggest that, as is currently demonstrated under the Common Rule, removing de-identified specimens from human subject requirements allows for safety and ethical

considerations while reducing administrative burden for investigators and streamlining effectiveness. The comments suggest there is a longstanding tradition of research using de-identified human tissue in a way that demonstrates adherence to the Belmont principles of justice, beneficence and respect for persons. Further the comments express the belief that requiring consent for tissue routinely archived would render a very large and crucial resource essentially off limits for research as most institutions/hospitals, particularly outside academia, do not include consent for surplus tissue use prior to surgery or tissue biopsy. The comments suggested that asking for consent retrospectively is very cumbersome, costly and may be perceived as intrusive by patients.

FDA Response: These comments are not related to the information collection or burden estimate. However, we have forwarded the comment to the appropriate program office for consideration.

Comment: A comment suggested that four hours per recordkeeper may be a significant underestimation of the burden of the information collection. The comment referenced Section V of the 2006 Guidance Section V and stated that the two-step process in that section amounts to both a general review of policies and procedures and a study-by-study investigational review board review to ensure compliance. The comment suggested that requiring reviews at the level of individual FDA investigations will lead to an aggregate of more than four hours per year per recordkeeper.

FDA Response: The comment was considered but FDA does not believe that the four-hour estimate is a significant underestimation given that these actions should not be a burdensome process for the recordkeeper.

Comment: The commenter opposed changing the default from "opt-in" to "opt-out" for patients to consent to their tissue being used for research. Although simple malformations, such as warts and tumors, may be useful to labs to fine-tune their tests, and although many (even most) patients might be willing to share this tissue, a significant minority of Americans hold beliefs about the human body that would prevent them from consenting, and all Americans likely assume that their tissue is destroyed (burned as medical waste) after procedures have been performed. The commenter believes that changing what happens without changing the public understanding of what happens is fundamentally dishonest. The commenter recognizes that obtaining consent is time-consuming, particularly when the patient does not speak English as a first language, or has other comprehension issues; however, the commenter believes no lab has a right to the tissue of an American citizen for its private, profit-making use.

FDA Response: The subject of the comment deals with sample acquisition, a step that happens in advance of the information communicated in this guidance. Therefore, patient “opt-in” versus “opt-out” is out of scope. This guidance describes the enforcement discretion policy FDA uses when sponsors choose to use de-identified samples for IVD medical device clinical trials.

9. Explanation of Any Payment or Gift to Respondents

No payment or gifts will be provided to respondents to this information collection.

10. Assurance of Confidentiality Provided to Respondents

This ICR does not collect personally identifiable information (PII). FDA's guidance document "Guidance on Informed Consent For In Vitro Diagnostic Device Studies Using Leftover Human Specimens That Are Not Individually Identifiable" informs sponsors, institutional review boards (IRBs), clinical investigators, and agency staff that the FDA intends to exercise enforcement discretion, under certain circumstances, with respect to its informed consent regulations under 21 CFR 812.2 (c) (3), for in vitro diagnostic device studies that are conducted using leftover specimens. Sponsors that follow this guidance should maintain written documentation demonstrating that they meet the circumstances outlined in the guidance. This information collection will be used only to assist clinical investigators, sponsors, and IRBs in conducting research with leftover specimens that are not individually identifiable. The guidance document explains what constitutes a not individually identifiable specimen.

FDA further determined this collection 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.

In preparing this Supporting Statement, FDA staff consulted with the FDA Privacy Office to ensure appropriate handling of information collected.

11. Justification for Sensitive Questions

This information collection does not include questions that are of a sensitive nature, such as, sexual behavior and attitudes, religious beliefs, and other matters that are commonly considered private.

12. Estimates of Annualized Burden Hours and Costs

12 a. Annualized Hour Burden Estimate

FDA bases its estimate on FDA's experience with the documentation burden associated with the Current Good Manufacturing Practices in the Quality System Regulation, 21 CFR part 820 (approved under OMB control number 0910-0073).

Estimated Annual Recordkeeping Burden					
Activity	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours
Recordkeeping regarding leftover human specimens that are not individually identifiable that are used in certain IVD studies	700	1	700	4	2,800

12b. Annualized Cost Burden Estimate

FDA estimates that the total cost to industry is $105,532 (2,800 hours x $37.69/hour). We expect the recordkeeping will be done by scientists. The mean hourly wage rate has been updated using the May 2017 Bureau of Labor and Statistics data for microbiologists, specifically (SOC Code Number 19-1022, http://www.bls.gov/oes/current/oes_nat.htm#19-0000). This adjustment has caused an increase of $2,520 to the annualized cost burden estimate.

Type of Respondent	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
Microbiologists	2,800	$37.69	$105,532

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

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

14. Annualized Cost to the Federal Government

Because the documentation is reviewed by an institutional review board (IRB) rather than FDA, there are no annualized costs to the Federal Government as a result of this guidance. The collections of information in 21 CFR parts 50 and 56, "Protection of Human Subjects; Recordkeeping Requirements for Institutional Review Boards," have been approved under OMB control number 0910-0130 and the collections of information in 21 CFR part 820, Quality System Regulation, have been approved under OMB control number 0910-0073.

15. Explanation for Program Changes or Adjustments

There are no program changes or adjustments to the estimated hour burden.

16. Plans for Tabulation and Publication and Project Time Schedule

The agency has no plans for tabulation or publication of information from this information collection.

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

FDA will display the OMB expiration date as required by 5 CFR 1320.5.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.