4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2012-N-0560]

Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Guidance on Informed Consent for in Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

DATES: Fax written comments on the collection of information by [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: To ensure that comments on the information collection are received, OMB recommends that written comments be faxed to the Office of Information and Regulatory Affairs, OMB, Attn: FDA Desk Officer, Fax: 202-395-7285, or emailed to oira_submission@omb.eop.gov. All comments should be identified with the OMB control number 0910-0582. Also include the FDA docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Amber Sanford, Office of Operations, Food and Drug Administration, Three White Flint North, 10A-12M, 11601 Landsdown St., North Bethesda, MD 20852, 301-796-8867, PRAStaff@fda.hhs.gov.

SUPPLEMENTARY INFORMATION: In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens That Are Not Individually Identifiable

OMB Control Number 0910-0582--Extension

FDA's investigational device regulations are intended to encourage the development of new, useful devices in a manner that is consistent with public health, safety, and compliant with ethical standards. Investigators should have freedom to pursue the least burdensome means of accomplishing this goal. However, to ensure that the balance is maintained between product development and the protection of public health, safety, and ethical standards, FDA has established human subject protection regulations addressing requirements for informed consent and institutional review board (IRB) review that apply to all FDA-regulated clinical investigations involving human subjects. In particular, informed consent requirements further both safety and ethical considerations by allowing potential subjects to consider both the physical and privacy risks they face if they agree to participate in a trial.

Under FDA regulations, clinical investigations using human specimens conducted in support of premarket submissions to FDA are considered human subject investigations (see 21 CFR 812.3(p)). Many investigational device studies are exempt from most provisions of part 812, Investigational Device Exemptions, under 21 CFR 812.2(c)(3), but FDA's regulations for the protection of human subjects (21 CFR parts 50 and 56) apply to all clinical investigations that are regulated by FDA (see 21 CFR 50.1, 21 CFR 56.101, and 21 U.S.C. 360j(g)(3)(A) and (D)).

FDA regulations do not contain exceptions from the requirements of informed consent on the grounds that the specimens are not identifiable or that they are remnants of human specimens

collected for routine clinical care or analysis that would otherwise have been discarded. Nor do FDA regulations allow IRBs to decide whether or not to waive informed consent for research involving leftover or unidentifiable specimens.

In the document entitled "Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens That Are Not Individually Identifiable," issued under the Good Guidances Practices regulation (21 CFR 10.115), FDA outlines the circumstances in which it intends to exercise enforcement discretion as to the informed consent regulations for clinical investigators, sponsors, and IRBs.

The recommendations of the guidance impose a minimal burden on industry. FDA estimates that 700 studies will be affected annually. Each study will result in one annual record, estimated to take 4 hours to complete. This results in a total recordkeeping burden of 2,800 hours ($700 \times 4 = 2,800$).

In the *Federal Register* of March 5, 2019 (84 FR 7906), FDA published a 60-day notice requesting public comment on the proposed collection of information. FDA received the following comments:

(Comment 1) Some comments strongly support further harmonization between the updated Common Rule and FDA regulations. Although the comments support 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 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 because 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.

(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 2) A comment suggested that 4 hours per recordkeeper may be a significant underestimation of the burden of the information collection. The comment referenced Section V of the 2006 Guidance 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 IRB 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 4 hours per year per recordkeeper.

(Response) The comment was considered but FDA does not believe that the 4-hour estimate is a significant underestimation given that these actions should not be a burdensome process for the recordkeeper.

(Comment 3) 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.

(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.

FDA estimates the burden of this collection of information as follows:

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

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

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

Based on a review of the information collection since our last request for OMB approval, we have made no adjustments to our burden estimate.

Dated: August 5, 2019.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

[FR Doc. 2019-17026 Filed: 8/7/2019 8:45 am; Publication Date: 8/8/2019]