UNITED STATES FOOD & DRUG ADMINISTRATION

Protection of Human Subjects and Institutional Review Boards

OMB Control Number 0910-0130 – Revision

SUPPORTING STATEMENT – **Part A: Justification**

1. Circumstances Making the Collection of Information Necessary

This information collection supports Food and Drug Administration (FDA, the agency, us or we) regulations governing requirements for informed consent and institutional review boards (IRBs) that are intended to protect the rights and safety of human subjects involved in FDA-regulated clinical investigations (21 CFR parts 50 and 56). The regulations in 21 CFR parts 50 and 56 apply to all clinical investigations regulated by FDA under sections 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355(i) or 360j(g)), as well as clinical investigations that support applications for research or marketing permits for products regulated by FDA, including food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products.

Under 21 CFR part 50, except under certain conditions, no investigator may involve a human being as a subject in FDA-regulated research unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. The elements of informed consent are provided in the regulations, along with related requirements for documentation and IRB approval of informed consent. Specifically, basic elements of the informed consent are set forth in § 50.25 and include a statement of the purpose and duration of a subject's participation in the research; a description of the procedures to be followed; identification of any experimental procedures; a description of risks, benefits, and appropriate alternative procedures or treatments; a description of extent to which confidentiality of records identifying the subject will be maintained; certain contact information; and a statement that participation is voluntary and may be discontinued at any time. Additional elements set forth in § 50.25 are required as appropriate. Exceptions to these requirements are governed by § 50.23, which requires both investigator and physician to certify in writing that the necessary elements for exception from general requirements have been satisfied; and § 50.24, which covers exception from informed consent requirements for emergency research. In accordance with § 50.27, informed consent must be documented, unless an IRB waives documentation as provided in § 56.109(c). Additional safeguards are required for children, as prescribed in subpart D (21 CFR parts 50.50 through 50.56) of the regulations.

Regulations in 21 CFR part 56 govern the composition, operation, and responsibilities of IRBs, including review and approval prior to the initiation of FDA-regulated clinical investigations and continuing review of such research. The regulations in 21 CFR part 56 also cover IRB administrative activities, including identification of types of IRB records that must be prepared and maintained. Required recordkeeping includes documentation requirements pertaining to written procedures, proposals reviewed, committee membership, meeting minutes, actions taken by the IRB, and correspondence, as well as other functional and operational aspects of the IRB.

Finally, the regulations describe administrative actions for non-compliance, including both disqualification of IRBs or IRB parent institutions, as well as reinstatement and alternative and additional actions.

We are revising the information collection by consolidating related elements currently approved under OMB Control No. 0910-0755. We believe that consolidating the information collection is appropriate and will improve our efficiency in support of administering laws and regulations for the protection and welfare of human subjects. In this ICR, we specifically account for burden we attribute to the requirements found in 21 CFR parts 50 and 56, consistent with OMB terms of clearance applicable to ICR Control No. 0910-0755:

Burden associated with 21 CFR § 50.25 (Elements of Informed Consent) and 21 CFR § 50.27 (Documentation of Informed Consent) is limited to the burden of development and approval by an institutional review board (IRB) of a site-specific informed consent document, and the documentation of informed consent. OMB does not grant approval for the content of individual consent forms that are reviewed and approved by IRBs and subsequently presented to research participants.

We therefore request OMB approval of the information collection provisions found in 21 CFR parts 50 and 56 and discussed in this supporting statement.

2. Purpose and Use of the Information Collection

The information collection is used to protect the rights and safety of human subjects involved in FDA-regulated research. We also use the information collection to support conducting audit inspections of IRBs to determine whether IRBs and clinical investigators are providing adequate protections to human subjects participating in clinical research we regulate.

Certain limited provisions in part 50, subpart B (informed consent of human subjects) and 21 CFR part 56 (IRBs) are currently approved under OMB control number 0910-0755. Those sections are:

50.24	Exception from Informed Consent Requirements for Emergency Research
50.25	Elements of Informed Consent
50.27	Documentation of Informed Consent
56.109(d)	Written statement about research when documentation of informed consent is waived
56.109(e)	IRB Written Notification to Approve or Disapprove Research
56.109(g)	IRB written statements to the sponsor about required public disclosures related to emergency research under 50.24
56.113	Suspension or Termination of IRB Approval of Research
56.120(a)	IRB Response to Lesser Administrative Actions for Noncompliance
56.123	Reinstatement of an IRB or Institution

As discussed above, we are now consolidating the provisions into this information collection.

The IRB must maintain documentation of its activities as required under 21 CFR 56.115. The records are maintained by IRBs to document that the IRB's responsibilities to protect the rights and welfare of human subjects in compliance with FDA regulations have been fulfilled and must be made accessible for inspection and copying to FDA at reasonable times and in a reasonable manner.

3. Use of Improved Information Technology and Burden Reductions

The regulations impose no technological burdens nor require standardized formats for respondents, and we encourage the use of automated technology.

4. Efforts to Identify Duplication and Use of Similar Information

We are unaware of duplicative information collection, although we maintain ICRs that cover other information collection burden for sponsors of and investigators conducting FDA-regulated studies involving human subjects. For example, our regulations in 21 CFR part 312 include investigator recordkeeping requirements for studies conducted under an investigational new drug application (IND) (21 CFR § 312.62). (Information collection provisions in part 312 are currently approved under OMB Control No. 0910-0014.) Similarly, recordkeeping requirements for investigators conducting studies under an investigational device exemption (IDE) in 21 CFR § 812.140 are currently approved under OMB Control Number 0910-0078.

5. Impact on Small Businesses or Other Small Entities

A substantial majority of IRB reviews are conducted at large institutions such as universities, medical schools, and research and teaching hospitals. The recordkeeping requires what FDA believes is the minimal documentation necessary to ensure both the effective operation of IRBs and implementation of human subject protection. Likewise, a substantial majority of clinical investigators conducting FDA-regulated research conduct those studies at large institutions such as universities, medical schools, and research and teaching hospitals. To assist respondents, FDA has developed and widely distributes a series of guidance documents to assist IRBs, clinical investigators and others concerned with the protection of research subjects to conform to the requirements in FDA regulations. For example, FDA has developed an "*Institutional Review Board Frequently Asked Questions Information Sheet*," available on its website at: https://www.fda.gov/RegulatoryInformation/Guidances/ucm126420.htm. Information is available regarding the agency's bioresearch monitoring program as well, which respondents may also find helpful. FDA has issued other guidance to assist respondents to the information collection including *Minutes of Institutional Review Board (IRB) Meetings,* available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/minutes-institutional-review-board-irb-meetings; and *Institutional Review Board (IRB) Written Procedures*, available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/institutional-review-board-irb-written-procedures/.

6. Consequences of Collecting the Information Less Frequently

The information collection schedule is consistent with existing laws and regulations, including 21 CFR parts 50 and 56.

7. Special Circumstances Relating to the Guidelines in 5 CFR 1320.5(d)(2)

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 the Federal Register of August 14, 2019 (84 FR 40421) we published a 60 day notice requesting comment on this proposed collection of information. We again invited public comment in our Federal Register notice of December 19, 2019 (84 FR 69748), however no comments have been received.

9. Explanation of Any Payment or Gift to Respondents

No payment or gift is provided to respondents.

10. Assurance of Confidentiality Provided to Respondents

The documentation obtained during IRB inspections rarely contains any sensitive or confidential information that has not been submitted to FDA (e.g., copies of research protocols which may be considered confidential and contain trade secret information). The material is kept confidential in accordance with 18 U.S.C. 1905, 21 U.S.C. 331(j), and 21 U.S.C. 360j(c).

11. Justification for Sensitive Questions

The documentation maintained and collected does not contain questions pertaining to sexual behavior, attitude, religious beliefs, or any other matters that are commonly considered private or sensitive in nature. Such data are more commonly contained in behavioral research, which FDA does not regulate. The identity of study subjects is rarely collected. Such sensitive information is treated as confidential and not released to third parties unless required by law or requested by Congress.

12. Estimates of Annualized Burden Hours and Costs

12a. *Annualized Hour Burden Estimate*

Respondents to the information collection include clinical investigators and IRBs or other persons subject to the requirements of 21 CFR parts 50 and 56. Based on a review of data, there are currently 2,520 IRBs overseeing FDA-regulated clinical research.

We therefore estimate the burden of the information collection as follows:

Our burden tables are organized to reflect one regulatory provisions per row. We have listed each provision as either a reporting burden, a recordkeeping burden, or a third-party disclosure burden in the tables below in a way we feel best reflects the operational aspect of the applicable provision.

We assume each of the 2,520 IRBs meets an average of 14.6 times annually and that approximately 40 hours of person-time per meeting are required to meet the IRB recordkeeping requirements of 21 CFR 56.115. We have reduced the estimate of average burden per response from 100 hours to 40 hours since last OMB review of the information collection, because we believe the original estimate of 100 hours has decreased with the use of electronic recordkeeping and new technologies available to maintain records. We estimate burden associated with recordkeeping responsibilities under 21 CFR parts 50 and 56 cumulatively, however we have itemized burden associated with certain of the regulatory provisions for purposes of providing a more detailed estimate.

We characterize our estimates of burden associated with 21 CFR 50.25, 56.109(d) and 56.109(e) as disclosure burdens. We estimate that eight IRBs per year will receive a request to review emergency research under § 50.24, thus requiring written notification under 21 CFR 56.109(g) from the IRB to the sponsor. We estimate that it will take an IRB approximately 1 hour to prepare each written statement, for a total of 2 hours per study. The total annual third-party disclosure burden for IRBs to fulfill this requirement is estimated at 16 hours.

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

21 CFR Section	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
56.113; suspension or termination of research	2,520	1	2,520	0.5 (30 minutes)	1,260
56.120(a); IRB response to lesser administration actions for noncompliance	7	1	7	10	70
56.123; reinstatement of an IRB or an institution	1	1	1	5	5
TOTAL			2,528		1,335

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

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

21 CFR Section	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
50.24; exceptions from informed consent for emergency research	8	3	24	1	24
50.27; documentation of informed consent	2,520	40	100,800	0.5 (30 minutes)	50,400
56.115; IRB records (documentation of IRB activities)	2,520	14.6	36,792	40	1,471,680
TOTAL			137,616		1,626,759

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

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
50.25; elements of informed consent	2,520	40	100,800	0.5 (30 minutes)	50,400
56.109(d); written statement about minimal risk research when documentation of informed consent is waived	2,520	2	5,040	0.5 (30 minutes)	2,520
56.109(e); written notification to approve or disapprove research	2,520	40	100,800	0.5 (30 minutes)	50,400
56.109(g) IRB written statement about public disclosures to sponsor of emergency research under 50.24	8	2	16	1	16
TOTAL			206,656		103,336

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

12b. *Annualized Estimated Cost Burden Estimate*

Using 2016 wage data from the Bureau of Labor Statistics, we estimate $85 per hour (mean salary of upper plus middle management, and clerical support, plus overhead and personnel benefits) for preparing and submitting the information requested. When multiplied by the total number of burden hours discussed above (1,731,430), we estimate the information collection costs respondents an average of $ 147,171,550 annually..

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

There are no capital costs, or operating and maintenance costs, associated with the collection of information.

14. Annualized Cost to the Federal Government

Periodically FDA investigators conduct bioresearch monitoring inspections of IRBs. Funding is allocated from existing bioresearch monitoring allocations and therefore we estimate no cost to the Federal government for the collection of information.

15. Explanation for Program Changes or Adjustments

The information collection reflects both changes and adjustments. We revised the information collection to include related elements found in other FDA regulations and discuss their applicability to our burden assessment above. Because of the operational aspects of the provisions, we feel consolidating the related information collection elements into one ICR will improve our ability to both administer the regulations and evaluate their attendant burden. In this request, our estimate reflects a decrease in the average number of annual responses by 1,947,770, but an increase in the average number of annual hours by 310,008. We feel this shows that most burden to respondents results from recordkeeping responsibilities described in part 56 (21 CFR 56). We note also that, upon OMB approval of this ICR, we will discontinue OMB control number 0910-0755, which currently accounts for 104,679 responses and 108,392 hours associated with recordkeeping requirements in 21 CFR part 56. We have also uploaded cost figures discussed both previously and with this submission so that they appear at www.reginfo.gov.

16. Plans for Tabulation and Publication and Project Time Schedule

The records maintained under this regulation are not expected to be published.

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

Display of OMB Expiration Date is appropriate.

18. Exceptions to the Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.