

UNITED STATES FOOD & DRUG ADMINISTRATION

Institutional Review Board Waiver or Alteration of Informed Consent for Minimal Risk Clinical Investigations – Final Rule

OMB Control No. 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) rulemaking RIN 0910-AH52. The regulations in 21 CFR parts 50 and 56 are intended to protect the rights and safety of human subjects involved in FDA-regulated clinical investigations and 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.

We are revising the information collection to include an exception from the requirement to obtain informed consent for certain minimal risk clinical investigations. The 21st Century Cures Act (Cures Act) (Pub. L. 114-255, section 3024) amended sections 505(i)(4) and 520(g)(3) of the Federal Food, Drug, and Cosmetic Act to provide FDA with the authority to permit an exception from informed consent requirements when the proposed clinical testing poses no more than minimal risk to the human subject and includes appropriate safeguards to protect the rights, safety, and welfare of the human subject. The rule will permit an IRB to waive or alter certain informed consent elements or to waive the requirement to obtain informed consent, under limited conditions, for minimal risk clinical investigations.

Unlike current FDA regulations, which allow for exception from the general requirements for informed consent only in life-threatening situations when certain conditions are met (21 CFR 50.23) or when the requirements for emergency research are met (21 CFR 50.24), HHS's "*Federal Policy for the Protection of Human Subjects*" (the Common Rule (82 FR 7149, January 19, 2017)) allows a waiver of informed consent for minimal risk research if specific criteria are met. The Common Rule criteria have been adopted and successfully employed for decades by numerous Federal agencies.¹ We believe that the final rule will both safeguard the rights, safety, and welfare of human subjects and enable minimal risk clinical investigations that may facilitate medical advances and promote public health. In addition, because some clinical research is subject to both FDA and the HHS requirements, we believe that harmonization of our waiver provision for minimal risk clinical investigations will help to provide clarity for and reduce burden on the research community by minimizing the need for separate processes for review of such requests.

We therefore request OMB approval of the information collection provisions found in the

¹ 45 CFR 46.116(f).

amended regulations and discussed in this supporting statement.

2. Purpose and Use of the Information Collection

The information collection is used to protect the rights and welfare 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.

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). The collections of information in part 312 are currently approved under OMB Control No. 0910-0014. Similarly, the collections of information pertaining to recordkeeping requirements for investigators conducting studies under an investigational device exemption (IDE) in 21 CFR § 812.140 are currently approved under OMB Control No. 0910-0078.

5. Impact on Small Businesses or Other Small Entities

The information collection poses no undue burden on 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 applicable statutory and regulatory authorities.

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

There are no special circumstances relating to the information collection.

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

In the *Federal Register* of November 15, 2018 (83 FR 57378), FDA issued a proposed rule to revise our informed consent regulations at part 50 (21 CFR part 50) to permit an IRB to waive or alter certain informed consent elements or to waive the requirement to obtain informed consent, under limited conditions, for certain FDA-regulated minimal risk clinical investigations. We stated in the rule that, “[t]his proposed rule refers to previously approved collections of information found in FDA regulations... . Therefore, FDA tentatively concludes the requirements in this document are not subject to additional review by OMB.” In developing the final rule, we determined that there are information collections contained in the rule that are subject to review by OMB under the PRA (44 U.S.C. 3501-3521). We discuss this more fully in our final rule and provide a summary of burden analysis in Q-12 of this supporting statement.

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

Consistent with 5 CFR 1320.5(d)(2)(vii), data will be kept private to the extent allowed by law:

The Privacy Act of 1974

In preparing this supporting statement, we consulted our Privacy Office to ensure appropriate identification and handling of information collected. This ICR does not collect personally identifiable information (PII) or information of a personal nature. This rule supports FDA’s IRB waiver or alteration of informed consent requirements for certain types of minimal risk clinical investigations. Typically, informed consent contains the name of the subject or his/her legally authorized representative. With this rule, the IRB may waive informed consent for a very small

segment of FDA-regulated research (those investigations that meet the criteria for the waiver). Because FDA does not collect PII, the ICR is not subject to the Privacy Act of 1974 and the requirements of the Privacy Act such as displaying a Privacy Act Statement on a collection form do not apply.

The Freedom of Information Act (FOIA)

Under FOIA (5 U.S.C. 552), the public has broad access to government documents. However, FOIA provides certain exemptions from mandatory public disclosure of government records (5 U.S.C. 552(b)(1-9)). FDA will make the fullest possible disclosure of records to the public, consistent with the rights of individuals to privacy, the property rights of persons in trade, and confidential commercial or financial information.

11. Justification for Sensitive Questions

The information collection does not include questions of a sensitive nature.

12. Estimates of Annualized Burden Hours and Costs

12a. *Annualized Hour Burden Estimate*

Description of Respondents: Respondents to the information collections include investigators who request waivers or alterations of informed consent under § 50.22 (table 2) and IRBs that review and approve FDA-regulated clinical investigations (table 3).

Table 1.--Estimated Third Party Disclosure and Burden for Waiver or Alteration of Informed Consent for Minimal Risk Clinical Investigations¹

21 CFR Part 50 (Protection of Human Subjects)	No. of Respondents	No. of Disclosures per Respondent	No. of Annual Disclosures	Average Burden per Record (h)	Total Hours
50.22 – development of request for waiver or alteration of informed consent for submission to IRB	551	1	551	1.0	551

¹ There are no capital or operating and maintenance costs associated with the information collection.

Our ability to provide a precise estimate for this burden is limited by the lack of information regarding the number of FDA-regulated clinical investigations for which a waiver or alteration of informed consent will be requested under new § 50.22 on an annual basis. Based on our review of information from ClinicalTrials.gov (<https://clinicaltrials.gov/>; accessed on June 21, 2022), we estimate that there will be, at most, 551 new FDA-regulated clinical investigations per year for which an investigator might request a waiver or alteration of informed consent under the new regulations at § 50.22. We do not anticipate that investigators will request waivers or alterations of informed consent for ongoing clinical investigations that are approved by an IRB before the effective date of the rule, and therefore, our estimate reflects burden we attribute to new clinical investigations. Our estimate of the annual number of studies for which a waiver or alteration of

consent under § 50.22 may be requested is based on an analysis of studies registered to the ClinicalTrials.gov databank as having started in 2021. This analysis focused on studies that, as registered, include a U.S. site, are not expanded access studies, do not have an IND or IDE, and study an FDA-regulated product (n=2201). This sample includes the studies registered to ClinicalTrials.gov most likely to be minimal risk clinical investigations but is not limited to such clinical investigations. Device studies reported on ClinicalTrials.gov as not having an IDE would likely include studies of “non-significant risk” devices that are conducted under the abbreviated IDE requirements (See 21 CFR 812.2(b)). However, “non-significant risk” and “minimal risk” are different concepts that serve different regulatory purposes, so “non-significant” risk device studies captured in our ClinicalTrials.gov sample may not meet the minimal risk criterion at § 50.22(a) for a waiver or alteration of consent. In addition, not all drug studies that are exempt from the requirement to have an IND would qualify as minimal risk. Thus, we expect that the sample of 2201 studies identified includes studies that are more than minimal risk. This sample may also include studies that would not be FDA-regulated clinical investigations, as defined at 21 CFR 50.3(c).

In addition, to qualify for a waiver, studies in this sample of potential minimal risk clinical investigations would need to meet all the requirements outlined in § 50.22, not just the “minimal risk” criterion. Many of these potential minimal risk investigations may be practicable to conduct without a waiver or alteration of informed consent and thus investigators would be unlikely to request a waiver or alteration for those studies. Clinical investigators and IRBs have implemented FDA’s general requirements for informed consent at Part 50 for decades; we do not expect clinical investigators to often propose, or for IRBs to often find, that it is impracticable to carry out a clinical investigation without a waiver or alteration of informed consent. Given these additional considerations, we estimate that, at most, an investigator might request a waiver or alteration of informed consent under new § 50.22 for approximately 25% (n= 551) of the investigations identified in our sample.

For this rule, we estimate that for each new clinical investigation for which a waiver or alteration of informed consent is requested under 21 CFR 50.22, one respondent (an investigator) will spend a total of 1.0 hours to prepare a request for a waiver or alteration of consent as part of a submission for IRB approval of proposed research (table 2).

Table 2.--Estimated Recordkeeping Burden for Waiver or Alteration of Informed Consent for Minimal Risk Clinical Investigations¹

21 CFR Part 56 (Institutional Review Boards (IRBs))	No. of Respondents	No. of Records per Response	No. of Annual Records	Average Burden per Record (h)	Total Hours
56.115 – IRB determination and documentation regarding waiver or alteration request	551	1	551	1.0	551

¹ There are no capital or operating and maintenance costs associated with the information collection.

As noted above, the accuracy of our estimate may be limited due to a lack of data on the numbers

of FDA-regulated clinical investigations for which a waiver or alteration will be requested, as FDA regulations have not provided for an exception from informed consent requirements for this type of research prior to the issuance of this rule. We intend to adjust our estimate of burden upon our evaluation of respondents' implementation of the final rule provisions. For purposes of assessing burden attendant to the rulemaking however, we estimate that for each new request, one IRB will spend a total of 1.0 hours to review the request and document its findings regarding whether the requested waiver or alteration satisfies the requirements under §§ 50.22 (table 23). This estimate includes 0.75 hours (45 minutes) for the IRB review of the request, and .25 hours (15 minutes) to document the IRB's decision regarding the request. We believe these IRBs are likely to document the findings required to approve the waiver or alteration request in IRB meeting minutes that they are required to maintain under existing requirements at § 56.115(a)(2), although the findings could be documented elsewhere in IRB records.

12b. Annualized Cost Burden Estimate

The rule will require clinical investigators and/or sponsor representatives of clinical investigations to draft requests for waivers or alterations of consent. The estimated net present value of document drafting costs associated with the rule are approximately \$3.8 million, with a lower bound of approximately \$1.9 million and an upper bound of approximately \$7.6 million, discounted at 3 percent over 10 years. At a 7 percent discount rate, the estimated net present value of costs is approximately \$3.4 million, with a lower bound of approximately \$1.7 million and an upper bound of approximately \$6.8 million. The annualized document drafting costs associated with the rule are approximately \$444.2 thousand at a 3 percent discount rate, with a lower bound of approximately \$222.1 thousand and an upper bound of approximately \$888.4 thousand. At a 7 percent discount rate, annualized costs are approximately \$480.7 thousand, with a lower bound of approximately \$240.3 and an upper bound of approximately \$961.3 thousand.

We anticipate that affected IRBs will incur additional costs associated with the time burden associated with review of waiver applications and recordkeeping burdens pertaining to the rule. The net present value of estimated review and recordkeeping costs is approximately \$14.9 million, with a lower bound of approximately \$7.4 million and an upper bound of approximately \$29.7 million, discounted at 3 percent over 10 years. At a 7 percent discount rate, the net present value is approximately \$12.2 million, with a lower bound of approximately \$6.1 million and an upper bound of approximately \$24.5 million. Annualized review and recordkeeping costs are approximately \$1.7 million, with a lower bound of approximately \$871.6 thousand and an upper bound of approximately \$3.5 million, at 3 and 7 percent discount rates.

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 information collection.

14. Annualized Cost to the Federal Government

We currently estimate \$8,750,000 in annual costs to the Federal government to administer requirements in 21 CFR parts 50 and 56, including the costs of this rulemaking.

15. Explanation for Program Changes or Adjustments

We estimate the rulemaking will result in an annual burden increase of 1,102 responses and 1,102 hours from recordkeeping and disclosure activity relating to the revised regulations in 21 CFR parts 50 and 56.

16. Plans for Tabulation and Publication and Project Time Schedule

This information collected will not be published or tabulated.

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

FDA will display the OMB control number as required by 5 CFR 1320.5.

18. Exceptions to the Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.