Supporting Statement for Protection of Human Subjects: Assurance of Compliance with Federal Policy/IRB Review/IRB Recordkeeping/Informed Consent/Consent Documentation

Background

The Office for Human Research Protections is requesting a three-year extension of information requirements in OMB No. 0990-0260, Protection of Human Subjects: Assurance of Compliance with Federal Policy/Institutional Review Board (IRB) Review/IRB Recordkeeping/Informed Consent/Consent Documentation.

The Federal Policy for the Protection of Human Subjects (also known as the Common Rule) adopted in June 1991 (56 FR 28001) establishes Federal policy for the protection of human subjects involved in Federally conducted or supported research. The Common Rule requires applicant and awardee institutions to establish procedures to report, disclose and maintain required information, including related to informed consent and assurance of the establishment of an IRB. The principal respondents for the information collection requirements in OMB No. 0990-0260 are IRBs.

A. Justification

1. Need and legal basis

Section 491(a) of Public Law (P.L.) 99-158 states that,

> The Secretary shall by regulation require that each entity which applies for a grant, contract, or cooperative agreement under this chapter for any project or program which involves the conduct of biomedical or behavioral research involving human subjects submit in or with its application for such grant, contract, or cooperative agreement assurances satisfactory to the Secretary that it has established (in accordance with regulations which the Secretary shall prescribe) a board (to be known as an "Institutional Review Board") to review biomedical and behavioral research involving human subjects conducted at or supported by such entity in order to protect the rights of the human subjects of such research.

The pertinent authorizing legislation is 42 U.S.C. 289.

On June 18, 1991, fifteen Federal departments and agencies, including HHS, adopted the Common Rule (56 FR 28001). HHS codification of the Common Rule is found at 45 CFR 46.

Pursuant to the requirement in P.L. 99-158, HHS promulgated regulations at 45 CFR part 46, subpart A, the basic HHS Policy for the Protection of Human Subjects. The June 18, 1991 adoption of the common Federal Policy (56 FR 28001) by 15 departments and agencies, including HHS, implements a recommendation of the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research which was established on November 9, 1974, by Pub. L. 95-622. The Common Rule is based on HHS regulations at 45 CFR part 46, subpart A, the basic HHS Policy for the Protection of Human Subjects published on January 26, 1981 (46 FR 8366).

As the Common Rule is based on the HHS regulations implementing P.L.99-158, the Common Rule echoes the same requirements set forth in this law in that it requires each institution engaged in research involving human subjects conducted or supported by any of the Common Rule departments or agencies to provide a written assurance satisfactory to the department or agency head that the institution, among other things, has established an IRB to review such research. The purpose of the IRB review is to ensure that the rights and welfare of human research subjects are adequately protected. To that end, the Common Rule requires that appropriate minutes of IRB meetings be maintained as documentation of the IRB review and approval and that an institution certify IRB review and approval to the departments and agencies conducting or supporting the research.

The Common Rule provides additional protections for human research subjects by including requirements for obtaining and documenting informed consent of the subjects. The Common Rule requires that informed consent to be sought from, and documented for, each subject, to the extent required by Sections 116 and 117, for all research to which the Common Rule applies.

On January 19, 2017, HHS and fifteen other Federal departments and agencies, revised the Common Rule to modernize, strengthen and make it more effective (82 FR 7149). The revised Common Rule includes some additional information collections, including: regarding the information that must be given to prospective research subjects as part of the informed consent process; allowing investigators to seek broad consent from a subject for storage, maintenance and secondary research use of identifiable private information and identifiable biospecimen; expanding the type of IRB activities for which records must be prepared and documented; and, adding a requirement to post consent forms for Common Rule department or agency-conducted or -supported clinical trials.

In this supporting statement, the term "pre-2018 Common Rule (or pre-2018

Requirements)" refers to subpart A of 45 CFR part 46 (i.e., the Common Rule) as published in the 2016 edition of the Code of Federal Regulations. The term "2018 Common Rule (or 2018 Requirements)" refers to the revised Common Rule as published in the July 19, 2018 edition of the Code of Federal Regulations. The 2018 Requirements published on January 19, 2017 (82 FR 7149) were amended on January 22, 2018 (83 FR 2885) and June 19, 2018 (83 FR 28497).

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The Federal departments and agencies that follow the Pre-2018 Requirements and the 2018 Requirements are listed below.

Pre-2018 Requirements

Common Rule Department or Agency Signatories:

Number	Department or Agency	CFR Citation
1	Department of Agriculture	7 CFR Part 1c
2	Department of Energy	10 CFR Part 745
3	National Aeronautics and Space Administration	14 CFR Part 1230
4	Department of Commerce	15 CFR Part 27
5	Agency for International Development	22 CFR Part 225
6	Department of Housing and Urban Development	24 CFR Part 60
7	Department of Justice	28 CFR Part 60
8	Department of Defense	32 CFR Part 219
9	Department of Education	34 CFR Partm97
10	Department of Veterans Affairs	38 CFR Part 16
11	Environmental Protection Agency	40 CFR Part 26
12	Department of Health and Human Services	45 CFR Part 46
13	National Science Foundation	45 CFR Part 690
14	Department of Transportation	49 CFR Part 11
15	Consumer Product Safety Commission	16 CFR Part 1028

Common Rule Department or Agency Executive Order or Statutory Mandate:

Number	Department or Agency	EO/Statutory Mandate
1	Department of Homeland Security	Pub. L. 108-458, title VIII, section 8306
2	Social Security Administration	Pub. L. 103-296, Section 106
3	Office of the Director of National Intelligence	Executive Order 12333

4	Central Intelligence Agency	Executive Order 12333

2018 Requirements

Common Rule Department or Agency Signatories[1]:

Number	Department or Agency	CFR Citation
1	Department of Homeland Security	6 CFR Part 46
2	Department of Agriculture	7 CFR Part 1c
3	Department of Energy	10 CFR Part 745
4	National Aeronautics and Space Administration	14 CFR Part 1230
5	Department of Commerce	15 CFR Part 27
6	Social Security Administration	20 CFR Part 431
7	Agency for International Development	22 CFR Part 225
8	Department of Housing and Urban Development	24 CFR Part 60
9	Department of Labor	29 CFR Part 21
10	Department of Defense	32 CFR Part 219
11	Department of Education	34 CFR Part 97
12	Department of Veterans Affairs	38 CFR Part 16
13	Environmental Protection Agency	40 CFR Part 26
14	Department of Health and Human Services	45 CFR Part 46
15	National Science Foundation	45 CFR Part 690
16	Department of Transportation	49 CFR Part 11
17	Consumer Product Safety Commission	16 CFR Part 1028

Common Rule Department or Agency Via Executive Order:

Number	Department or Agency	EO/Statutory Mandate
1	Office of the Director of National Intelligence	Executive Order 12333
2	Central Intelligence Agency	Executive Order 12333

2. Purpose and Use of the Information

Information reported to the Federal departments and agencies under the Common Rule with respect to a satisfactory assurance is used to ensure that an institution engaged in

[1] Department of Justice intends to become an official signatory.

nonexempt research involving human subjects conducted or supported by a Common Rule department or agency has (1) established adequate administrative policies and procedures for protecting the rights and welfare of human subjects in research, and (2) accepts that responsibility. Other reporting requirements are used to: assess whether the institution is following the established procedures; ensure that Federal funds are not expended for unapproved human subjects research; and, determine if the approved status of an awarded grant, contract, or cooperative agreement should be reviewed, with the ultimate goal of maintaining or increasing human subject protections.

The following information collections required by the Common Rule are included in this information collection request:

Section 103(b)(5) [Pre-2018 Requirements]/108(a)(4) [2018 Requirements] *Reporting* - Specifies certain situations which must be reported by the investigator and/or other institutional official(s) to the IRB, appropriate institutional officials, the department or agency head, and OHRP, HHS, or any successor office, or the equivalent office within the appropriate Federal department or agency.

Purpose: To ensure that the IRB and individuals responsible for the protection of human subjects are made aware of situations occurring during the research that trigger the need for them to take further action in discharging their responsibilities to protect the rights and welfare of human subjects participating in federally-conducted or –supported research.

Section 109(d) [Pre-2018 and 2018 Requirements] *Disclosure* - Specifies the procedures for an IRB to notify the investigators and institutions in writing of its decision to approve or disapprove proposed research activities, or of modifications required to secure IRB approval of the research activities.

Purpose: Provides individuals responsible for conducting the research with the information necessary to initiate the research or to take required actions before initiation of the research is permitted.

Section 113 [Pre-2018 and 2018 Requirements] *Reporting* - Specifies that any suspension or termination of IRB approval must be reported to the investigator, appropriate institutional officials, and the department or agency head and that such reports include a statement of the reasons for the IRB's action.

Purpose: To ensure that individuals responsible for the protection of human subjects are made aware of IRB actions regarding the research that trigger the need for them to take further action in discharging their responsibilities to protect the rights and welfare of human subjects participating in federally-conducted or –supported research.

Section 115(a) [Pre-2018 and 2018 Requirements] *Recordkeeping* - Specifies the documentation of IRB activities, including: copies of all research proposals reviewed; minutes of IRB meetings; records of continuing review activities [including the rationale for conducting continuing review of research that otherwise would not require continuing review as described in section 109(f)(1) of the 2018 Requirements]; copies of all correspondence between the IRB and the investigators; a list of IRB members in the same detail as described in section 103(b)(3) [Pre-2018 Requirements]/108(a)(2) [2018 Requirements]; written procedures for the IRB in the same detail as described in section 103(b)(4) and (5) [Pre-2018 Requirements]/108(a)(3) and (4) [2018 Requirements; statements of significant new findings provided to subjects, as required by section 116(b)(5) [Pre-2018 Requirements]/116(c)(5) [2018 Requirements]; the rationale for an expedited reviewer's determination under section 110(b)(1)(i) [2018 Requirements] that research appearing on the expedited review list described in section 110(a) [2018 Requirements] is more than minimal risk; and, documentation specifying the responsibilities that an institution and an organization operating an IRB each will undertake to ensure compliance with the requirements as described in section 103(e) [2018 Requirements]. Section 115(b) [Pre-2018 and 2018 Requirements] stipulate that records required by the Common Rule must be retained for at least three years, and records relating to research that is conducted must be retained for at least three years after completion of the research. All records shall be accessible for inspection and copying by authorized representatives of the department or agency conducting or supporting the research at reasonable times and in a reasonable manner.

Adequate documentation of IRB activities also requires records of IRB determinations required by subparts B, C, and D: i.e., (1) in subpart B, the conditions under 45 CFR 46. 204 (Research involving pregnant women or fetuses.), 45 CFR 46.205 (Research involving neonates.), 45 CFR 46.206 (Research involving, after delivery, the placenta, the dead fetus or fetal material.), and 45 CFR 46.207 (Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates.), are met; (2) in subpart C, the conditions under 45 CFR 46.305 (Additional duties of the Institutional Review Boards where prisoners are involved.) and 45 CFR 46.306 (Permitted research involving prisoners.), are met; and, (3) in subpart D, the conditions under 45 CFR 46.404 (Research not involving greater than minimal risk), 45 CFR 46.405 (Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.), 45 CFR 46.406 (Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.), and 45 CFR 46.407 (Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.), are met.

Purpose: Provides a means for verification by the Common Rule departments and agencies that substantive regulatory requirements for operation of IRBs and conduct of research involving human subjects have been fulfilled.

Section 116 (a) and (b) [Pre-2018 Requirements]/116(b), (c) and (d) *Disclosure* - Specifies the general requirements for, and basic elements of, informed consent in section 116 (a) [Pre-2018 Requirements]/116(b) [2018 Requirements]. Additional elements of informed consent, when appropriate, are found in section 116(b) [Pre-2018 Requirements]/116(c) [2018 Requirements]. Section 116(d) [2018 Requirements] specifies elements of broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens.

Purpose: Provides human subjects with information on which to base their independent decisions regarding whether or not they choose to take the risks involved in the research in light of the potential benefits which may result.

Section 116(h) [2018 Requirements] *Disclosure* – Specifies that for each clinical trial conducted or supported by a Federal department or agency, one IRB-approved consent form must be posted on a publicly available Federal website.

Purpose: Improves the quality of consent forms in federally funded research by assuring that the forms eventually would become subject to public scrutiny and provide useful models for others.

Section 117 *Disclosure* - Specifies how informed consent is to be documented.

Purpose: Provides verification that the human research subjects have been provided information on which to base their independent decisions regarding whether or not they choose to take the risks involved in the research in light of the potential benefits which may result.

Section 117(c)(2) [Pre-2018 and 2018 Requirements] *Disclosure* – Specifies that in cases in which the informed consent documentation is waived, the IRB may require the investigator to provide subjects or legally authorized representatives with a written statement regarding he research.

P*urpose*: Provides subjects with written information about the research in cases when the subjects have not signed an informed consent form (that would include information about the research).

3. <u>Improved Information Technology</u>

The Common Rule imposes no technological or standard format requirements for respondents. We encourage automated technology if possible.

4. Efforts to Identify Duplication

The Common Rule establishes the only Federal standards for the performance of federally conducted or supported research involving human subjects.

5. Small Businesses

Support of research activities involving human subjects extends to small businesses. The committee that developed the Common Rule considered ways to reduce the burden on small businesses or organizations that receive Federal support and determined that it was not feasible to do so. Institutions not having on file approved assurances for the proposed research (likely to be small organizations) generally do not have to certify IRB review until certification is requested by the agency or department sponsoring the research generally only when an award is expected to be made.

6. Consequences of Collecting the Information Less Frequently

The reporting of IRB approval is required with the submission of an application or proposal for research funding, or at such later date as specified by the federal department or agency sponsoring the research. This is necessary to ensure that federally-conducted or -supported research involving human subjects is subjected to the continuing IRB review and approval that is required by the Common Rule at least once per year, except as described in section 109(f) of the 2018 Requirements, as the obligation to protect human subjects is an ongoing responsibility and not a one-time effort. Changes in research protocols, new scientific or medical findings or innovations, as well as preliminary results or ongoing research, may change the degree of risks to the subjects or the subjects' willingness to continue participation in the research; therefore, IRB review is required to be conducted at least annually so that the rights and welfare of the human research subjects are protected throughout the research project. Reporting of the date of that review, and approval with the application describing any changes, notifies the department or agency conducting or supporting the research of IRB approval of the continued compliance of the protocol. Within HHS, the FWA form approved by OMB for use through August 31, 2023 (OMB No. 0990-0278) must be renewed every five years instead of every three years prior to June 2011. Other reporting requirements in the Common Rule are on occasion.

The regulations require that minutes of each IRB meeting be taken and kept. The IRB's continuing review, as indicated above, is required annually. Less frequent review would compromise protection of research subjects.

7. Special Circumstances

There are no special circumstances.

8. Federal Register Notice/Outside Consultation

Public comments were solicited in the *Federal* Register on April 14, 2021 (86 FR 19627) for a 60-day period. No comments were submitted.

9. Payment/Gift to Respondents

No payment or gifts are provided to respondents.

10. Assurance of Confidentiality

The database used to maintain and store IRB registration information, known as the Human Assurance Tracking System (HATS), uses Microsoft SQL Server tables stored on a server that is hosted and maintained by the Center for Information Technology, National Institutes of Health. The HATS application screens and associated IRB registration tables/server utilize a username/password and appropriate session variables to access and modify the IRB registration data. Without the appropriate username/password, unauthorized users will not gain access to the IRB registration database. IRB registration database tables will never be provided outside of OHRP. Requests for IRB registration information from the database are fulfilled via printed reports or disk files containing extracted information.

The public can access some IRB registration information from the internet, e.g., IRB organization and its IRB(s) name, number and location (city and state or country) and expiration date) via the internet search screens found on the OHRP website at http://ohrp.cit.nih.gov/search/search.aspx?styp=bsc. The public would need to contact OHRP to request non-public IRB registration information (e.g., the name or contact information of an IRB organization's head official, contact person, or IRB chairperson).

11. Sensitive Questions

None of the information collection requirements in the Common Rule are of a sensitive nature.

12. Estimates of Annualized Burden Hours and Cost

Burden estimates for reporting to OHRP: unanticipated problems involving risks to subjects or others; serious or continuing noncompliance with 45 CFR part 46 or the

determinations or requirements of the IRB; and, suspension or termination of IRB approval of research as required in section 103(b)(5) of the pre-2018 Requirements and section 108(a)(4) of the 2018 Requirements are accounted for in an OHRP new information collection request submission (Incident Report Form) currently pending OMB approval. Burden estimates for IRB review and certification requirements in section 103(f) of the pre2018 and 2018 Requirements are accounted for in an OHRP information collection request submission to OMB for re-approval of Control Number 0990-0263 (Approved for use through June 30, 2021). Burden estimates regarding IRB establishment and IRB membership provisions in sections 103(b)(2) and 107 of the pre-2018 Requirements and sections 107 and 108 of the 2018 Requirements are accounted for in the OHRP information collection request submission to OMB that was approved in Control Number 0990-0279 (Approved for use through February 28, 2022).

12a. Annualized Hour Burden Estimate

Respondents to this information collection include IRBs, investigators and other persons or entities subject to the Common Rule requirements. As of February 23, 2021, there are 5,063 active IRB organizations with 5,943 IRBs registered with OHRP. We are rounding the active registered IRBs to be 6,000.

The burden tables are organized to include specific regulatory provisions in each row for Pre-2018 Requirements and/or 2018 Requirements information collections. Table 1 regulatory provisions are identified as a reporting burden, table 2 regulatory provisions are identified as a recordkeeping burden and table 3 regulatory provisions are identified as a third-party disclosure burden.

Table 1-Estimated Annual Reporting Burden

Common Rule Provision	No. of Respondents	No of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
.103(b)(5), .113 [Pre2018 Requirements]/.108(a)(4), .113 [2018 Requirements] - Incident Reporting, Suspension or Termination of IRB approval Reporting	5,200	1	5,200	1	5,200
TOTAL			5,200		5,200

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Table 2 –Estimated Annual IRB Recordkeeping Burden

Common Rule Provision	No. of Respondents	No of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
.115 [Pre-2018 and 2018 Requirement] – Preparation and documentation of IRB activities	6,000	16	96,000	12	1,152,000
TOTAL			96,000		1,152,000

Table 3 – Estimated Annual Third-Party Disclosure Burden

	No. of Respondents	No of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
.109(d) [Pre-2018 and 2018 Requirements] – Written notification of IRB approval or disapproval of research	6,000	25	150,000	0.5	75,000

.46.116(a) and (b) (Pre-2018 Requirements)/ .46.116 (b), (c) and (d) [2018 Requirements] – Elements of informed consent and broad consent	6,000	25	150,000	0.5	75,000
.46.116(h) – [2018 Requirements] – Posting clinical trial consent form	100	3	300	0.5	150
.117(a) [Pre-2018 and 2018 Requirements] – Documentation of informed consent	6,000	25	150,000	0.5	75,000
.117(c)(2) [Pre-2018 and 2018 Requirements] – Written statement about the research when informed consent	6,000	10	60,000	1	60,000
	No. of Respondents	No of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
documentation is waived					
TOTAL			510,300		285,150

12b. Annualized Estimated Cost Burden

We estimate an average hourly wage of $43 per hour. When multiplied by the total number of burden hours (1,442,350), we estimate the information collection costs respondents an average of $62,021,050 annually.

13. Capital Costs (Maintenance of Capital Costs)

There are no direct capital costs to respondents.

14. Annualized Cost to the Federal Government

We estimate that cost to the Federal government for the collection of information will be 1,992,000.

15. Program or Burden Changes

The information collection reflects changes, for Pre-2018 Requirements and 2018 Requirements. The burden hours increased by 304,120 hours and $35,611,450.

16. Publication and Tabulation Dates

There are no plans to publish or tabulate the information.

17. Expiration Date

Display of OMB expiration date is appropriate.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.

LIST OF ATTACHMENTS

Attachment 1 - Legal Authorities
- a. 42 U.S.C. Section 289
- b. 56 F.R. 28001 (Common Rule)
- c. 45 CFR part 46

- Legal Authorities

Attachment 1

a. 42 U.S.C. Section 289

TITLE 42 – The Public Health and Welfare

CHAPTER 6A – PUBLIC HEALTH SERVICE

SUBCHAPTER III – NATIONAL RESEARCH INSTITUTES

Part H – General Provisions

INSTITUTIONAL REVIEW BOARDS; ETHICS GUIDANCE PROGRAM

Sec. 491. [289](a) The Secretary shall by regulation require that each entity which applies for a grant, contract, or cooperative agreement under this Act for any project or program which involves the conduct of biomedical or behavioral research involving human subjects submit in or with its application for such grant, contract, or cooperative agreement assurances satisfactory to the Secretary that it has established (in accordance with regulations which the Secretary shall prescribe) a board (to be known as an Institutional Review Board) to review biomedical and behavioral research involving human subjects conducted at or supported by such entity in order to protect the rights of the human subjects of such research.

(b)(1) The Secretary shall establish a program within the Department of Health and Human Services under which requests for clarification and guidance with respect to ethical issues raised in connection with biomedical and behavioral research involving human subjects are responded to promptly and appropriately.

(2) The Secretary shall establish a process for the prompt and appropriate response to information provided to the Director of NIH respecting incidences of violations of the rights of human subjects of research for which funds have been made available under this Act. The process shall include procedures for the receiving of reports of such information from recipients of funds under this Act and taking appropriate action with respect to such violations.

(*July 1, 1944, ch. 373, title IV, Sec. 491, as added Pub.L. 99-158, Sec. 2, Nov. 20, 1985, 99 Stat. 873.*)

- Legal Authorities

Attachment 1

a. 56 F.R. 28001 (Common Rule), Pre-2018 Requirements
b. HHS 2018 Requirements, Access here: https://www.ecfr.gov/cgibin/retrieveECFR?gp=&SID=83cd09e1c0f5c6937cd9d7513160fc3f&pitd=20180719&n=pt45.1.46&r=PART&ty=HTML

- Legal Authorities

Attachment 1

c. 45 CFR part 46

Access here: https://www.ecfr.gov/cgi-bin/retrieveECFR?gp=&SID=83cd09e1c0f5c6937cd9d7513160fc3f&pitd=20180719&n=pt45.1.46&r=PART&ty=HTML