NIH Policy Manual

3014-205 - Requirements for IRB Submissions

Issuing Office: OD/OIR/OHSRP **Phone:** (301) 402-3713

Approving Official(s): DDIR

Release Date: 10/01/2020 ?
Partial Revision Date: 11/30/2022 ?
Technical Revision Date: 4/16/2021 ?

Transmittal Notice

1. **Explanation of Material Transmitted:** NIH Human Research Protection Program (HRPP) policies have been revised to comport with the revised DHHS Common Rule (45 CFR 46) and to reflect the newly consolidated IRB structure within the NIH Intramural Research Program (IRP). This policy describes the requirements for investigators for submissions to the NIH IRB, to NIH IRB members when reviewing IRB submissions, and IRBO staff when reviewing research that may be exempt under 45 CFR 46. Upon implementation, this policy fully supersedes the following HRPP Standard Operating Procedures (SOPs): SOP 5 Research Activities with Human Data/Specimens, SOP 6 Determinations, Including Exemptions Made by the Office of Human Subjects Research Protections (OHSRP), SOP 8 Procedures and Required Documentation for Submission and Initial Review of Protocols, SOP 9 Continuing Review by the Convened IRB, SOP 10 Amendments to IRB-approved Research, SOP 11 Suspensions and Terminations of IRB Approval and Administrative Holds and SOP 11A Closure of an IRB-approved protocol. Upon implementation, this policy partially supersedes SOP 16 Reporting Requirements for Unanticipated Problems, Adverse Events and Protocol Deviations. **Partial Revision Date**: 11/30/2022 These revisions update terminology to comport with the implementation of Huron PROTECT electronic IRB system.
2. **Filing Instructions:**

- **Insert:** NIH Manual Chapter 3014-205, dated 10/01/2020, **Partial Revision Date:** 11/30/2022
- **Implementation Date:** 10/12/2020

1. **PLEASE NOTE:** For information on:

- The current policies can also be found at: https://irbo.nih.gov/confluence/display/ohsrp/Policy.
- Content of this chapter, contact the issuing office listed above.

- NIH Policy Manual, contact the Division of Compliance Management, OMA, on (301) 496-4606, or enter this URL: https://oma.od.nih.gov/DMS/Pages/Manual-Chapters.aspx

A. Purpose

1. Describes the requirements for submissions for exempt or non-exempt human subjects research to facilitate review by the NIH Institutional Review Board (IRB) (i.e., review by the convened IRB, expedited procedures, limited IRB procedures, or exempt procedures).

B. Scope

1. This policy applies to:

    a. NIH investigators when the NIH IRB is the Reviewing IRB, or when the human subjects research may be exempt from IRB review.
    b. Non-NIH investigators when the NIH is the Reviewing IRB.
    c. The NIH IRB, including those experienced IRB members designated to conduct expedited review, limited IRB review or exempt review (referred to as designated reviewers).

        I. Note that certain Office of IRB Operations (IRBO) staff members are also IRB members. These include:

            i. IRBO staff designated as reviewers, to conduct expedited or limited IRB review.
            ii. IRBO staff designated as reviewers to review research that is possibly exempt under 45 CFR 46.101 (Pre-2018 Common Rule) or 45 CFR 46.104 (2018 Common Rule).

    d. For information about NIH requirements when the NIH relies on an external Reviewing IRB, see *Policy 3014-105 IRB Reliance*.

C. Policy

1. The Principal Investigator (PI) must ensure that all required materials (e.g., the required documentation and information collected in the electronic IRB system) are submitted to the IRB in a timely manner to determine its approvability.

    a. When the NIH IRB is the Reviewing IRB, all required materials must be submitted through the NIH electronic IRB system.

2. When conducting its review, the convened IRB, or designated reviewer (using expedited, limited IRB, or exempt procedures) will review the submitted materials in

order to determine that the regulatory and policy requirements for approval of research are met, or whether more information is needed to make a determination.
3. Submissions that are incomplete may be withdrawn by IRBO from IRB consideration.
4. When closing research at the NIH, the PI must provide assurance to the IRB that the maintenance and future use of specimens will be consistent with the plan described in the protocol and with the informed consent(s).
5. The PI, Sponsor, or the Institute/Center (IC) may prematurely close the research, or the IRB may suspend or terminate its approval. (See *Policy 3014-204 Levels of IRB Review and Criteria for IRB Approval of Research*.)
6. Institute/Center leadership has the authority to direct a PI to close a study with the IRB; and if deemed necessary, IC leadership may submit the study closure, or other submissions, to the IRB on behalf of the PI.

D. Definitions

OHSRP has developed a comprehensive glossary of definitions that describe the terms listed below. The glossary can be found at the following link: NIH IRP HRPP Policy Glossary

Note: There *may be more than one definition per term*, so please review terms carefully to make sure they match the terms listed below. Qualified terms are indicated with a parenthetical qualification. When reviewing a definition, be sure that you are reviewing the appropriate definition that links to this policy. To further assist the reader, each term in the glossary cites the relevant policy number(s) indicating where the term is utilized

Definitions demarcated with (***Pre-2018 Common Rule***) apply to research approved by an IRB (or deemed to be exempt, or for which no Institutional Review Board (IRB) review was required under the regulations) prior to the effective date of the 2018 Common Rule (January 21, 2019).

Definitions demarcated with (***2018 Common Rule***) apply to all research approved by an IRB (or deemed to be exempt, or for which no IRB review was required under the regulations) on or after January 21, 2019 and to research transitioned to the 2018 requirements in accordance with NIH Human Research Protection Program (HRPP) policy.

1. Amendment (See Modification)
2. Continuing review (Pre-2018 Common Rule Definition)
3. Continuing review (2018 Common Rule Definition)
4. Exempt Research
5. Initial review
6. Modification (previously referred to as an Amendment)
7. Reviewing IRB
8. Study Closure

E. Responsibilities and Requirements

1. **General Requirements for Submissions to the NIH IRB**

This section describes the general requirements for submissions to the NIH IRB and the required components of those submissions. Sections *E.2.-E.4.* below describe the responsibilities of the parties (PI, Office of IRB Operations (IRBO) staff, or the NIH IRB) with regard to these submissions.

a. **Required materials for Initial Review of non-exempt human subjects research:** For all new applications submitted via the electronic IRB system regarding non-exempt human subjects research (whether reviewed by the convened IRB or by a designated reviewer using expedited procedures), the following materials must also be submitted:

I. Research protocol, including a description of the data and safety monitoring plan (See NIH protocol templates: https://irbo.nih.gov/confluence/display/ohsrp/Protocol+Templates);
II. Informed consent and/or assent documents (e.g., consent, parental permission, information sheets, verbal script), as applicable;
III. Initial Scientific Review with Chief Scientific Officer (CSO) approval or waiver (*Policy 3014-106 Ancillary Reviews*);
IV. For covered protocols, the Deputy Ethics Counselor (DEC) clearance. (*See Policy* Policy 3014-102 Investigator Conflict of Interest and Government Royalties);
V. Recruitment materials, as applicable (e.g., email text, flyers, posters, scripts, social media ads) (Policy 3014-302 Subject Recruitment and Compensation);
VI. Study instruments used to collect data from research subjects (e.g., surveys, interview forms, questionnaires, assessments), as applicable;
VII. Ancillary committee approval(s) (e.g., Radiation Safety Committee, Institutional Biosafety Committee, etc.), as applicable (*Policy 3014-106 Ancillary Reviews)*;
VIII. If the NIH investigator will be conducting research at a non-NIH site, documentation from the non-NIH site indicating permission for the NIH investigator to conduct research at that site (e.g., a letter of support), as applicable (See *Policy 3014-105 IRB Reliance*.);
IX. For new applications involving investigational drugs or devices, or off-label use of a drug or device, submission to the IRB must follow the IND and IDE requirements described in *Policy 3014-500 Research Involving Drugs, Biologics, and Nutritional Products* or *Policy 3014-501 Research Involving FDA Regulated Devices*, as applicable.
X. For initial review involving multi-site research for which the NIH IRB is the Reviewing IRB, the documentation must include:

i. A model protocol that includes a description of the research activities which are occurring at each site;
ii. A model informed consent document(s) when the NIH is initiating the research;

iii. The model informed consent(s) for participating sites;
iv. Confirmation from each of the participating sites that the institutional requirements of the relying institution have been met; and
v. Any other documents or information that the IRBO requests.

b. **Required materials for initial review of exempt human subjects research:** The following materials must be submitted along with the appropriate application in the electronic IRB system:

I. Research protocol (e.g., the *Protocol Template for Prospective Data Collection* or *Protocol Template for Secondary Research*); and
II. When the research involves prospective collection of data:

i. Document outlining the elements of informed consent (e.g., consent form, information sheet, verbal script, etc.);
ii. Recruitment materials, (e.g., flyers, posters, scripts, social media ads) (Policy 3014-302 Subject Recruitment and Compensation), as applicable; and
iii. Study instruments used to collect data from research subjects (e.g., surveys, interview forms, questionnaires, assessments).

III. Any other documents or information that the IRBO requests.

c. **Required materials for Continuing Review (CR) of non-exempt human subjects research:** For CR of non-exempt human subjects research (whether reviewed by the convened IRB or by a designated reviewer using expedited procedures), in addition to the appropriate application in the electronic IRB system the following materials must be submitted:

I. The most recent IRB-approved protocol;
II. The most recent IRB-approved informed consent/assent documents, as applicable;

i. In addition, if a subject was enrolled in the past year, provide a redacted copy of the last NIH signed consent(s)/assent(s) for each of the IRB-approved informed consent/assent forms used in the previous review period.

III. For covered protocols, indication of the Deputy Ethics Counselor (DEC) clearance. (See Policy 3014-102 Investigator Conflict of Interest and Government Royalties.)
IV. Documentation to support the data and safety monitoring plan, as applicable, and if not previously submitted prior to the time of continuing review (e.g., data safety monitoring report(s));
V. Any audit reports not previously submitted to the IRB; and
VI. Any other documents or information that the IRBO requests.

d. **Required materials for modifications to non-exempt human subjects research:** For modifications to previously approved non-exempt human subjects research (whether reviewed by the convened IRB or by designated reviewer using expedited procedures), in addition to the appropriate application in the electronic IRB system the following materials must be submitted:

I. Revised protocol, as applicable;
II. Revised informed consent and/or assent documents (e.g., consent, parental permission, information sheets, verbal script), as applicable;
III. For covered protocols, for which a new NIH investigator is being added, documentation of the Deputy Ethics Counselor (DEC) clearance (See *Policy* Policy 3014-102 Investigator Conflict of Interest and Government Royalties*.);*
IV. Any other documents or information that the IRBO requests; and
V. When the NIH IRB is the Reviewing IRB and the PI is adding a participating site, whether to initiate multi-site research or to expand an existing multi-site protocol, the modification must include the following documentation:

i. Letter of support from the participating site where the research will be conducted indicating that local site requirements have been met;
ii. The NIH model consent form template that includes the participating site's required site-specific language (e.g., subject injury language, conflict of interest language), as applicable;
iii. Confirmation from the participating site that the institutional requirements of the relying institution have been met; and
iv. Any other documents or information that the IRBO requests.

e. **Required materials for modifications to exempt human subjects research:** For modifications to previously approved research determined to be exempt (whether reviewed by exempt procedures or limited IRB procedures), in addition to the appropriate application in the electronic IRB system, the following materials must be submitted:

I. Revised research protocol (e.g., see the *Protocol Template for Prospective Data Collection* or *Protocol Template for Secondary Research*) as applicable;
II. When the proposed research involves prospective collection of data, include the following documentation, as applicable:

i. Revised document outlining the elements of informed consent (e.g., consent form, information sheet, verbal script, etc.);
ii. Revised recruitment material, as applicable (e.g., email text, social media ads, flyers, posters, scripts, etc.), as applicable; (See Policy 3014-302 Subject Recruitment and Compensation.) and
iii. Revised study instruments used to collect data from research subjects (e.g., surveys, interview forms, questionnaires, assessments); and

III. Any other documents or information that the IRBO requests.

f. **Requirements for Reporting Research Events for exempt and non-exempt human subjects research:** Please see *Policy 3014-801 Reporting Research Events* regarding submissions of reportable research events (e.g., UPs, Protocol Deviations, Adverse Events, Deaths, and Non-Compliance) to the IRB.

g. **Required materials for submission of study closure for non-exempt human subjects research:** When all study activities are complete including data analysis, or when the research is being prematurely closed (see *Policy 3014-204 Levels of IRB Review and Criteria for IRB Approval of Research*), the study closure must be submitted via the Continuing Review application in the electronic IRB system. In addition, the following materials must also be submitted:

I. Provide assurance to the IRB that the disposition and future use of any data and specimens is consistent with the description in the protocol and in the informed consent(s);
II. Draft communication for subjects regarding premature closure of the study, if applicable, and not already approved by the IRB, as part of an modification.
III. A high-level summary (not a line item listing) of minor protocol deviations and AEs/SAE that do not meet the definition of an unanticipated problem (UP) that have occurred since the time of the last IRB review. (See *Policy 3014-801 Reporting Research Events.)*
IV. Any other documents or information that the IRBO requests.

2. **Principal Investigator Responsibilities and Requirements**

a. **The PI is responsible for:**

I. Ensuring the completeness of submissions to the NIH IRB consistent with the requirements of this policy.
II. Ensuring all submissions to the NIH IRB will be via the NIH electronic IRB system using the appropriate study application (e.g., initial review, continuing review, or modification) and supporting documentation (e.g., protocol, informed consent/assent documents, and other documents as descrived above) consistent with the type of review sought, see E.1. above.

b. When the NIH is relying on an external Reviewing IRB, the NIH PI/Lead Site Investigator must first submit all required model documents (e.g., the model protocol and model consents) to the IRBO, via the NIH electronic IRB submission system, for institutional review consistent with the requirements outlined in *Policy 3014-105 IRB Reliance and Collaborative Research.*

3. **Office of IRB Operations Responsibilities and Requirements**

a. Office of IRB Operations (IRBO) is responsible for screening all submissions (e.g., initial reviews, modifications, or continuing reviews) to the NIH IRB (whether for review by the convened IRB or by designated review using expedited or limited IRB or exempt procedures), or when conducting an institutional review of NIH research when

the NIH is relying on an external Reviewing IRB as outlined in *Policy 3014-105 IRB Reliance and Collaborative Research*.

b. At its discretion, the IRBO may administratively withdraw submissions from IRB consideration when the PI is non-responsive to requests from the IRB or from IRBO staff for 30 calendar days. The investigator will be notified by the IRBO if the submission is administratively withdrawn.
c. The submission components described in this policy are considered IRB records and will be retained by the IRBO consistent with the requirements of *Policy* Policy 3014-206 Maintenance of Records.

4. **IRB Responsibilities and Requirements**

a. When conducting its review, the convened NIH IRB or, the designated reviewer (using expedited, limited IRB or exempt procedures), must review the submission materials in order to determine that all regulatory and policy requirements for approval of research are met. (See *Policy 3014-204 Levels of IRB Review and Criteria for IRB Approval of Research*.)

F. References

1. **Federal Regulations**

HHS: 45 CFR 46

FDA: 21 CFR parts 50, 56, 312 and 812

2. **NIH Policy**

Policy 3014-102 Investigator Conflict of Interest and Government Royalties

Policy 3014-105 IRB Reliance

Policy 3014-106 Ancillary Reviews

Policy 3014-204 Levels of IRB Review and Criteria for IRB Approval of Research

Policy 3014-206 Maintenance of Records

Policy 3014-302 Subject Recruitment and Compensation

Policy 3014-500 Research Involving Drugs, Biologics, and Nutritional Products

Policy 3014-501 Research Involving FDA Regulated Devices

Policy 3014-801 Reporting Research Events

3. **Guidance and Tools**

Office for Human Research Protections (OHRP) guidance: *Continuing Review Guidance (2010)*

Protocol Template for Prospective Data Collection

Protocol Template for Secondary Research

NIH protocol templates: https://irbo.nih.gov/confluence/display/ohsrp/Protocol+Template