Rhode Island Department of Health

Institutional Review Board For the Protection of Human Subjects

Guidance for the Submission of Applications & Progress Reports to the IRB

For Additional Information Contact:
RIDOH.IRB@health.ri.gov

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TABLE OF CONTENTS

Jurisdiction of the RIDOH Institutional Review Board

The Rhode Island Department of Health (RIDOH) operates an Institutional Review Board (IRB) that reviews proposals for research on human subjects under a Federal Wide Assurance (FWA). The IRB's jurisdiction extends to all research proposals involving RIDOH staff, data, or resources. IRB jurisdiction applies, but is not limited to, proposals where:

1. An employee* of RIDOH serving as Principal Investigator, Co-Investigator or in any role with scientific responsibility in the research project, whether paid or in-kind.

2. An employee* of RIDOH is funded under the grant, contract, cooperative agreement, or other award supporting the research project.

3. An employee* of RIDOH engaged directly in recruitment, data collection, or intervention with human research subjects or in any other capacity requiring informed consent, assent, or for which informed consent is usually required but has been waived as allowed in federal human subjects' protection regulations.

4. RIDOH provides confidential data, in which an individual is identified directly or indirectly, to the project.

5. RIDOH provides any financial or in-kind support for the performance of the research project.

6. An employee* of RIDOH will be an author of a manuscript resulting from the research that will be submitted for publication and that will include the employee's affiliation with the Department.

*For the purposes of this policy, employees of the Rhode Island Department of Health are defined as (1) full-time and part-time employees in the state personnel system (2) contract employees and (3) Public Health Scholars.

Relying on an External IRB

The RIDOH IRB may rely on the IRB of an external organization, that possesses an FWA, if the IRB of the external organization is better prepared to review the research, or the research is federally funded and subject to NIH's single IRB mandate. The RIDOH IRB reserves the right to sever as the IRB of record for any project seeking to use RIDOH data that is not publicly available, regardless of the investigators home institution, unless operating under the IRB approval of a federal agency.

Procedures For Conducting The Initial Review Of Research

All formal review processes will be subject to the *Code of Federal Regulations, Title 45, Public Welfare, Department of Health and Human Services, Part 46, Protection of Human Subjects* and future amendments thereof. To examine the categories which may qualify research activities for exempt status, please refer to Appendix D of this document.

Exempt Human Subjects Research Policy

It is the policy of the Rhode Island Department of Health IRB that all research activities under its jurisdiction involving human subjects, or protected health information, be reviewed to determine whether the proposed activities are exempt from the requirements of 45 CFR 46 and 21 CFR 56. Only the Chair of the IRB, or their designee, may determine which activities qualify for exempt status. Under no circumstances does an investigator or non-IRB member have the authority to make a determination on a project's exempt status, or commence project activities, without consulting the IRB.

Exempt research activities, while not necessitating the need for IRB oversight, are still subject to the same human rights protections and ethical standards outlined in the Belmont Report. Selection of participants should be equitable, unless specifically studying a targeted demographic, and all reasonable efforts should be made to assure the privacy of the participant. Regardless of exemption status, if there are any interactions with individuals participating in the study the IRB will make an assessment as to whether a consent process is necessary. In some instances, your exemption status may be contingent on consent processes being in place.

Determination of exempt status can be achieved through the IRB's formal application process, or through consultation with the IRB Chair or their designee. Only the IRB Chair, or their designee, may waive the application submission requirement if they believe they have enough information to assess exempt status. The IRB reserves the right to request a formal application for any activity involving human subjects or protected health information.

Amendments to Exempt Research Studies

In some instances, an amendment to previously exempt activities may disqualify the exempt status. Any deviation from the original proposed activities, that may impact exempt status, shall be brought before the IRB. Examples that may alter exempt status include but are not limited to: inclusion of protected at-risk demographics, collection of identifiable information, or inclusion of populations that would trigger the Department's Small Numbers Policy.

Limited IRB Review

Exempt categories 2, 3, 7, and 8 shall require a limited IRB review whenever subjects are identifiable, either directly or indirectly, by the investigator; this includes secondary research using previously acquired data or biospecimens. In these instances, a formal application to the IRB will be required to assess possible risk factors associated with the use or transfer of identifiable, or protected health, information.

Research Involving Pregnant Women or Neonates

Research involving pregnant women, human fetuses, and neonates may qualify for exempt status provided the conditions of the exemption are met.

Research Involving Prisoners

Research involving prisoners, except for activities targeting broad populations of which prisoners are included, will not qualify for exemption status. In these instances, a formal application shall be submitted to the IRB.

Research Involving Children

Exempt categories 2, 3, 7, and 8 shall not apply to research involving children with the following exception:

- Category 2(i) and (ii) may be eligible for exemption status if the investigator is not a participant in the activities being observed.

All proposed activities involving the use of children shall require a formal application to the IRB.

Expedited Review of Human Subject Research Policy

Activities failing to meet the criteria for exemption status, or activities requiring a limited IRB review, will necessitate a formal application be submitted, electronically, to the IRB. The IRB may use an expedited review procedure to assess proposed activities that meet any of the following criteria:

- Research that involves no more than minimal risk and can be classified as one of the expedited review categories authorized by 45 CFR 46.110 and 21 CFR 56.110
- Minor changes/amendments to previously approved research
- Research requiring a limited IRB review

Please note, activities are not automatically deemed to be "minimal risk" simply because they meet one of the expedited review categories. These categories merely authorize an expedited review of the proposed activities, not their approval.

The expedited review process may not be used when identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented to minimize the risks associated with an invasion of privacy, breach of confidentiality, or data leak.

Expedited Review Process

In addition to the RIDOH approved IRB application template, formal applications must include any of the below supplemental documents when applicable:

1. Any informed consent, or assent, documents that will be utilized in addition to all survey forms, questionnaires, or interview questions when applicable.

2. An "Assurance of the Principal Investigator" form. If the Principal Investigator is a student, the student's faculty sponsor should sign the form.

3. If the research involves a cooperating agency, institution, school district, or other organization, a letter of agreement to participate in the research, on official letterhead, is also required. Research that is to be conducted in foreign countries requires a letter of agreement from an appropriate official or cooperating institution.

4. When seeking data that is owned by RIDOH, a completed Data Request Agreement must accompany the application prior to review. If data is requested from the Department, this form tells the IRB that (1) the proposal has been vetted by the appropriate data holder (2) the data request was deemed appropriate for the study and (3) upon IRB approval the data holder agrees to release the requested data to the PI. Proposals that require RIDOH data will **not** be reviewed without this form.

In instances where a project is not granted an exemption status, the PI, and all researchers involved in the proposed work, must show evidence of successfully completing CITI training (or equivalent) with their application materials. The board must also be made aware of any researcher added to the study, that will have access to identifiable or protected health information, after approval. Submission of their CITI certification will be required prior to the individual commencing any study related activities.

IRB Review Determinations

Expedited Review

Once all required and supplemental materials are received by the IRB administrator (e-mail listed below), the IRB Chair, or an experienced IRB member, will review the proposed activities. The reviewer will make one of the following determinations:

1) Exempt from the requirements of 45 CFR 46
   - The reviewer has concluded that your research activities satisfy one of the Exempt categories outlined in 45 CFR 46
2) Approved as minimal risk research
   - The reviewer has concluded that your research activities met the requirements for expedited review and pose no more than minimal risk to study participants.
3) The proposed activity does not qualify as human subjects research and does not require IRB review
   - The proposed activities either do not involve human subjects, or do not constitute "research" as defined in 45 CFR 46.
4) Approval of proposed amendments
   - Changes to previously approved protocols impart no additional risk to human subjects and may be incorporated into the study protocol.
5) Forwarded for full IRB review
   - The reviewer believes the proposed activities impart more than minimal risk to human subjects and the proposal will be forwarded to the convened IRB for approval determination.
6) Revisions and/or additional information required
   - The proposal, as submitted, is either incomplete or will require revisions to the study design prior to receiving IRB approval.

Research may not be disapproved during the expedited review process. The reviewer may make recommendations to the investigator on how to modify their research design to allow for approval under one of the exempt categories or meet the standards for minimal risk.

If the reviewer feels the proposal poses more than minimal risk to the human subjects, involves protected populations, or that the data being requested from RIDOH is more than what is necessary to complete the study objectives, then they reserve the right to forward the application for Full Board Review.

Convened IRB Review

When reviewing a research application, the Convened IRB may also render the following additional determinations :

1) Disapproval of proposed activities
   - The convened IRB has decided that the proposal poses too great a risk to human subjects, or that the study design is flawed and in need of significant revision.
2) Approved as reasonable risk research
   - While more than minimal risk may be present in the study design, the IRB has concluded the all in-good-faith efforts to minimize risk have been implemented and the risk is appropriate given the study's potential need/benefit.
3) Continuing review required
   - The IRB will require progress reports pertaining to this study to assure risk continues to be assessed and minimized. The due date of these progress reports will be listed on the study's approval letter.

Notification

Investigators will be notified of an IRB decision electronically using a RIDOH approved decision template. Comments which highlight the factors leading to a decision will also be communicated using this form.

Oversight of Expedited Review

The entirety of the IRB is notified once a decision has been rendered during the expedited review process. Any member of the IRB has the right to request an application come before the full IRB regardless of the expedited review decision. While these instances are exceedingly rare; once initiated, research activities may not commence until the full Board is able to review the proposal and render a decision.

Expedited Review of Protected Populations

Pregnant Women, Human Fetuses, and Neonates

- Studies meeting Expedited Category 1 will be forwarded to the Convened IRB for review. If approved, the IRB will also make an assessment as to whether continuing review of these studies may be done through Expedited procedures.

Prisoners

- Research involving prisoners as the main subject population will be reviewed by the Convened IRB.

Children/Minors

- Research involving children may be reviewed through the Expedited Review procedure provided no more than minimal risk is posed to the participant.

E-Mail all application materials to: RIDOH.IRB@health.ri.gov

Approval Expiration, Continuing Review, and Study Modifications

Approval Expirations

For instances where continuing review is not requires, IRB approval will be in effect for the duration of the study provided no modifications to the originally approved protocol are necessary. The IRB should be informed of the closeout of any IRB approved study.

Continuing Review

When a proposal is approved, the convened IRB will decide whether the investigator needs to provide an update, or progress report, to the IRB throughout the course of the study. This will typically occur if the IRB has determined that the study poses more than minimal risk to human subjects, that potential conflicts of interest could exist, or the study utilizes FDA regulated components. Moreover, the IRB will assess the PIs prior engagement with the Board and may require continuing review if a history of non-compliance in their research practice is noted.

Regardless of whether continue review is required, it remains the responsibility of the investigator to alert the IRB of any unforeseen consequences, compliance issues, or modifications as it relates to their study.

When continuing review is required, the investigator will be provided a progress report template that shall be utilized to satisfy this requirement.

Modifications to Research

Modifications to research that has been approved by Expedited Review or a convened IRB may be approved by the expedited review process if the modifications fall within an expedited review category and do not pose an increased risk to subjects.

Confidentiality, Privacy, and Research Risk

Many research proposals submitted to the RIDOH Institutional Review Board involves the use of personally identifiable, confidential information housed within various Department databases. If the requested data is deidentified, or if there is no intent to contact the individuals whose information is being used, these proposals may be eligible for exemption from informed consent requirements; or reviewed under the expedited procedure. Such proposals should address the following issues in their IRB submissions:

1. Determine whether the proposed use of the data is research on human subjects as defined in the federal regulations governing human subject's protection. (See Appendix A).

2. Specify the risks and benefits of participating in the research for the human subjects. There are often no direct benefits to individuals whose confidential data is accessed. Risks may often include inadvertent and purposeful release of confidential data on an individual. Such release may occur through release of sufficient descriptive information as to allow identification, even when no identifiers are released.

3. Minimize the risks to human subjects in the design and conduct of the research. For use of existing data, this means that:
    a. The minimum amount of confidential information is requested that is necessary to perform the research.
    b. The information is accessible to and handled by the minimum number of personnel possible.
    c. Identifiers are removed from the database or the database is returned to the owner as soon as no longer needed.

4. Data that are published or otherwise released are aggregated so that no individual can be identified either directly or indirectly through knowledge of non-confidential data items.

5. Specify measures to protect data when on computers and when stored on electronic media. Also describe any data linkages that would result in anonymous data becoming identifiable to an individual.

6. If any contact is proposed with an individual identified through access to a RIDOH database, the issues of informed consent become relevant, and all protocols and forms must be reviewed in addition to measures to protect confidentiality.

The Informed Consent Process and General Requirements

Informed consent should be considered a process that may require continual review; it is not just a legal document.

Informed consent must be obtained only under such circumstances that provide the prospective subject, or the subject's representative, sufficient opportunity to consider participation in the research project and where the possibility of coercion or undue influences is minimized.

The Informed Consent Statement:

1. Must be written in a language understandable to the subject or representative.

2. Shall not contain any language by which the subject waives any of his or her rights.

3. Shall not contain any language that releases the principal investigator or the sponsoring agency from liability for negligence.

4. Should include a statement that verifies the signatory is over 18 years of age or that the representative has the legal authority to provide assent for the study participant.

The Informed Consent Statement should follow the format and outline given on the next page, as appropriate. When the subject is a minor and the parent or guardian's consent is sought, space for the parent or guardian's signature should be provided. If the subject is an adult requiring guardian consent, space for the guardian's signature should be provided. Alternatively, where it is necessary to separate the consent of the parent/guardian from the assent of the minor or non-consenting adult, separate forms should be used for each.

Two copies of the Informed Consent statement must be signed; one copy is to be retained by the individual (or his/her representative/guardian), and one copy is to be kept by the principal investigator. (NOTE: the signature page may not be completely separated from the text of the informed consent.)

For further guidance, see the "Informed Consent Information" section on the OHRP website.

Sample Informed Consent Form

Title of Project:

Introductory section should begin with words to this effect:
You have been asked to take part in a research project described below. The researcher will explain the project to you in detail. You should feel free to ask questions. If you have more questions later, {P.I.}, the person mainly responsible for this study, { Phone }, will discuss them with you. You must be at least 18 years old to be in this research project (if appropriate).

Description of the project:
You have been asked to take part in the study that {here describe the nature of the study and the purpose of the research}.

What will be done:
If you decide to take part in this study here is what will happen: {explanation of what will happen to the subject; how long the subject will be involved in the study; and state what portions, if any, are considered experimental. Explain alternative procedures, if any}.

Risks or discomfort:
{Explain any risks or discomfort that might reasonably be expected to happen. If there are no risks or discomforts, state that here}.

Benefits of this study:
{Describe benefits to the subject, or to others, of this study. If of no direct benefit to the subject, include a sentence to the following effect:} Although there will be no direct benefit to you for taking part in this study, the researcher may learn more about { }. (NOTE: payment given to the subject for participation in the study is not a benefit, it is a recruitment incentive.)

Confidentiality:
{Describe the way confidentiality of records identifying the subject will be maintained. Use words to the following effect, if appropriate:} Your part in this study is confidential. No information will be released that identifies you by name. All records will {describe how records are to be maintained}. {Or, if the study involves information that legally must be reported to government agencies, then include the following:} My part in this study is confidential within legal limits. The researchers and the sponsoring agency will protect your privacy, unless they are required by law to report information to city, state or federal authorities, or to give information to a court of law. Otherwise, none of the information will identify you by name. All records will be {describe how they are to be maintained}.{Alternatively, if the study is anonymous, then this should be stated here. Indicate to the subject how anonymity will be preserved.}

In case there is any injury to the subject: (If applicable)
{Explain whether any medical or other treatment is available if injury occurs, and who to contact; use words to this effect:} If this study causes you any injury, medical treatment will be provided to you through { }, and this treatment will be paid for by { }. To report any injury that happens because you agreed to be in this study, you should write or call { }.

Decision to quit at any time:
{Use words to the following effect:} The decision to take part in this study is up to you. You do not have to participate. If you decide to take part in the study, you may quit at any time. Whatever you decide will in no way {penalize you} {affect your benefits, medical care}{etc.} {insert appropriate language}. If you wish to quit, you simply inform {name and phone number of principal investigator} of your decision.

Rights and Complaints:
{Use words to the following effect:} If you have any questions later about your rights as a participant in this research, or if you are not satisfied with the way this study is performed, you may speak with {P.I.'s Name} or with {name and phone of individual}, anonymously, if you choose. In addition, you may contact { }, who is the Administrator of the Institutional Review Board of the Rhode Island Department of Health, at { }.

You have read the Consent Form. Your questions have been answered. Your signature on this form means that you understand the information and you agree to participate in this study.

Signature of Participant	Signature of Researcher
Typed/printed Name	Typed/printed name
Date	Date

CONSENT FORM
(Name of Project)

TEAR OFF AND KEEP THIS FORM FOR YOURSELF

Dear Participant:
You have been asked to take part in the research project described below. If you have any questions, please feel free to call (PI, phone number), the person mainly responsible for this study. The purpose of this study is to (state purpose). Responses to these items will be (state how

responses will be collected and how confidentiality will be maintained).

YOU MUST BE AT LEAST 18 YEARS OLD to be in this research project or to consent to your child's participation.

If you decide to take part in this study, your participation will involve (describe procedures) pertaining to (state appropriate information).

The possible risks or discomforts of the study are minimal, although you may feel some embarrassment answering questions about private matters (delete last phrase if it is not appropriate for your project).

Although there are no direct benefits of the study, your answers will help increase the knowledge regarding (state appropriate information).

Your part in this study is confidential. That means that your answers to all questions are private. No one outside the project can know if you participated in this study or know any information about your participation. Scientific reports will be based on group data and will not identify you or any individual as being in this project.

The decision to participate in this research project is up to you. You do not have to participate and you may quit at any time.

Participation in this study is not expected to be harmful or injurious to you. However, if this study causes you any injury, you should call the "IRB Administrator" at the Rhode Island Department of Health, {phone #}.

If you have any more questions or concerns about this study, you may contact (PI) at (phone #). You are at least 18 years old. You have read the consent form and your questions have been answered to your satisfaction. Your filling out the survey implies your consent to participate in this study.

If these questions are upsetting and you want to talk, please use the phone numbers below: (appropriate in cases where questions are of a sensitive nature):

(Names and phone numbers of resources available, e.g., Counseling Center, Women's Resource Center, AA, etc.). Thank you, (Name of Investigator)

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RIDOH IRB Members

CHAIR

Louis Marchetti, PhD, TC(NRCC)
Supervising Clinical Laboratory Scientist – State Health Laboratories

VICE-CHAIR

Vacant

FULL BOARD MEMBERS

Internal – Department of Health Staff

- Jolayemi Ahamiojie, MPH – Center for Health Promotion
- Roseann Giorgianni – Office of Vital Records
- James McDonald, MD, – Board of Medical Licensure
- Louis Marchetti, PhD, TC(NRCC) – State Health Laboratories
- Rachael Sardinha, BS – RIDOH Academic Institute

External – Community Members

- Colleen Fontana, BA
- John Fulton, PhD, Epidemiologist
- Vivian Weisman, MSW

FOR ADDITIONAL INFORMATION

For general information involving human subjects' protection, visit the website for the Office for Human Research Protections (OHRP) in the U.S. Department of Health and Human Services:
http://www.hhs.gov/ohrp

For documents relating to human subject's protection, including -The "Belmont Report" Regulations for the Protection of Human Research Subjects (45 CFR 46) Informed Consent Information visit the following website:
https://www.hhs.gov/ohrp/regulations- and-policy/index.html

For guidance with human subjects protection issues in public health, see the human subjects protection website at the Centers for Disease Control and Prevention:
https://www.cdc.gov/od/science/integrity/hrpo/index.htm

For information on federal certificates of confidentiality, which protect confidential information collected on research subjects from access through most federal, state, and local legal actions, such as subpoenas, see the following website:
https://www.hhs.gov/ohrp/regulations-and-policy/guidance/certificates-of-confidentiality/index.html

For Rhode Island's Confidentiality of Healthcare Communications and Information Act (Rhode Island General Laws Chapter 5-37.3) and specifically for requirements relating to the release of medical records (Section 5-37.3-4(d)) see:
http://webserver.rilin.state.ri.us/Statutes/TITLE5/5-37.3/5-37.3-4.HTM

Appendices

A. Does the Project Include Research Involving Human Subjects?

B. Research Involving Human Subjects Who Are Afforded Special Protections

C. Minors as Research Participants

D. Research exempt from IRB review

E. Research eligible for expedited review

Appendix A: Does the Project Include Research Involving Human Subjects

The Rhode Island Department of Health (RIDOH) Institutional Review Board (IRB) is established to review the procedures for protection of human subjects in all research projects that involve RIDOH staff, data, or other resources. The principal purpose of IRB review is to assure that the procedures for obtaining informed consent from human research subjects are properly established and administered.

To that end, the RIDOH IRB is mandated to review only those projects and programs that, in whole or part, meet the definition of research on human subjects, as presented in the federal regulations governing protection of human subjects (Title 45, Code of Federal Regulations, Part 46). The definitions are as follows:

Research means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities.

Human subject means a living individual about whom an investigator (whether professional or student) conducting research:

> (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
>
> (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

Interaction includes communication or interpersonal contact between investigator and subject.

Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).

Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

If a project or program, or any component of a project or program, does not meet both of these definitions, it is not subject to IRB review. It is the responsibility of the principal investigator (PI) of a project to obtain IRB review in all cases where appropriate. The PI may choose not to submit a project to the IRB if he/she believes it does not meet the federal definitions. However, this decision should be made in conjunction with either the chair or vice-chair of the IRB. The chair, vice-chair, members, and staff of the RIDOH IRB are available to investigators for consultation on the necessity of submitting specific projects for IRB review.

Appendix B: Research Involving Vulnerable Populations

Certain categories of human research subjects are afforded special protections under federal regulations because they are at greater risk of adverse consequences and/or because they require special consideration in the informed consent process. These categories are:

1. Pregnant women, Fetuses, and Neonates
2. Prisoners
3. Children.

The special protections afforded each of these categories of human subjects are detailed in Subparts B, C, and D of the federal regulations regarding the protection of human subjects, 45 CFR 46.

[Note: The National Institutes of Health (NIH) have instituted policies supporting diversity in the selection of human research subjects, for the purpose of maximizing the applicability of research results to all relevant populations. Investigators performing NIH-sponsored research projects should be aware of these policies and, for some groups, the impact of the policies on informed consent procedures. The policies are "Inclusion of Children in Research" and "Inclusion of Women and Minorities in Research" and can be found at the NIH web site "grants.nih.gov/grants/oprr/library_human.htm" under the heading "National Institutes of Health (NIH) Information."]

Appendix C: Minors As Research Participants

Children are more vulnerable than other research participants "...because of their more limited cognitive competencies and experiential backgrounds, which constrain their capacities to understand and defend their rights as research participants and to make responsible decisions concerning research participation. They are also vulnerable because of their limited social power, which impairs their ability to exercise independent decision-making concerning research participation..." (Thompson, 1990). Because of these limitations, special caution is advised in the preparation and review of protocols involving children as subjects. These include:

Consideration of the developmental level of the individual in the determination of "minimal risk": It is usually assumed that vulnerability in children decreases with age. However, there are conditions in which vulnerability increases or peaks at certain ages. For example, children's increasing self-awareness or adolescents' sensitivity to their changing bodies may make older children more vulnerable than younger children.

Considerations in obtaining informed consent or assent: It is clear that consent is required from the parent or guardian. Less clear are the requirements for the child's assent. Although children cannot consent to research, they do have the right to refuse to participate. It is recommended that the following be delineated in obtaining assent from children:

That assent be required and obtained in writing from the child unless there is a clear, written justification for not obtaining assent.

That there be a clear means of documenting how assent is obtained, and by whom. Where appropriate, a separate form should be drafted with language appropriate to the child's developmental level.

Explanation of and process for quitting or withdrawal from the research: Since children tend to be acquiescent to adult wishes and are often reluctant to speak up when uncomfortable, special attention must be given to processes for quitting or withdrawal from research. Along with the usual statements in the informed consent form, the researcher is advised to:

Be cognizant of signs of discomfort shown by the child throughout the interview or testing procedures, and periodically inquire about the child's reactions or feelings.

Include procedures for withdrawal that address the above considerations.

Appendix D: Research Exempt From IRB Review

Projects that do not meet the definition of research or do not involve human subjects as defined in Appendix A are exempt from IRB review. For projects that do involve research on human subjects, the following categories are exempt from review, per 45 CFR 46.101(b).

1. Research, conducted in established or commonly accepted educational settings, that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

2. Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:
    (i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
    (ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or
    (iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §46.111(a)(7).

3. (i) Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:
    (A) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
    (B) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

(C) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §46.111(a)(7).

(ii) For the purpose of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

(iii) If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

4. Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

(i) The identifiable private information or identifiable biospecimens are publicly available;

(ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;

(iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b); or

(iv) The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C.

3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 *et seq.*

5. Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.
    (i) Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal Web site or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

6. Taste and food quality evaluation and consumer acceptance studies:
    (i) If wholesome foods without additives are consumed, or
    (ii) If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

7. Storage or maintenance for secondary research for which broad consent is required: Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if an IRB conducts a limited IRB review and makes the determinations required by §46.111(a)(8).

8. Secondary research for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met:
    (i) Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with §46.116(a)(1) through (4), (a)(6), and (d);
    (ii) Documentation of informed consent or waiver of documentation of consent was obtained in accordance with §46.117;
    (iii) An IRB conducts a limited IRB review and makes the determination required by §46.111(a)(7) and makes the determination that the research to be conducted is within the scope of the broad consent referenced in paragraph (d)(8)(i) of this section; and (iv) The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent an investigator from abiding by any legal requirements to return individual research results.

Appendix E: Research Eligible for Expedited Review

Applicability:

A. Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.
B. The categories in this list apply regardless of the age of subjects, except as noted.
C. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects= financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.
D. The expedited review procedure may not be used for classified research involving human subjects.
E. IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review--expedited or convened--utilized by the IRB.
F. Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

Research Categories

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
    a. (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
    b. Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
    a. (a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
    b. from other adults and children [2], considering the age, weight, and health of the

subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

3. Prospective collection of biological specimens for research purposes by noninvasive means.

   Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.
4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

   Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject=s privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.
5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)
6. Collection of data from voice, video, digital, or image recordings made for research purposes.
7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural

beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

8. Continuing review of research previously approved by the convened IRB as follows:
    a. where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
    b. where no subjects have been enrolled and no additional risks have been identified; or
    c. where the remaining research activities are limited to data analysis.
9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified